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LOBAR PNEUMONIA.

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LOBAR PNEUMONIA.

Synonyms.—Croupous pneumonia, Fibrinous pneumonia, Pneumonitis, Lung Fever.

The lung differs from all other structures in having two separate circulations: the nutritive, supplied from the left side of the heart through the bronchial arteries, and the functional, supplied from the right side of the heart through the pulmonary artery. This double circulation underlies all the phenomena of pneumonia, and must be recognized in any definition of the disease, as without it the disease itself could not exist.

Definition.—*Lobar pneumonia is an acute disease in which a specific parasite invades the air cells of one or more pulmonary lobes, where it grows in a fibrinous medium exuded from the functional capillaries, and generates a toxin that infects the system at large.*

The local process causes consolidation of the affected area by filling the air cells with the effused material, which, material is afterwards removed, leaving the structure of the lung intact.

The general infection is marked by fever, which, in a typical case, begins with a chill, and after a duration of from four to nine days ends abruptly by crisis.

In most cases a local dry pleuritis is excited, the phenomena of which are added to those of the pneumonia proper.

Death may take place from the virulence of the infection, from loss of respiratory surface, from exhaustion of the right heart, from consecutive asthenia, from complications, or from a combination of two or more of these causes.

Symptoms.

A brief sketch of the principal clinical features of the disease will be useful as affording a preliminary view of the field to be examined.

The attack may be preceded by prodromes to be hereafter described, but as a rule the first complaint of the patient is of a pain in the chest, usually in the mammary region. This is often very severe, and by restricting the movements of the ribs renders the respiration superficial and rapid. A chill more or less severe follows,

or in many cases precedes, the pain. The chill varies from a mere creeping sensation to a heavy and prolonged rigor, as severe as in a case of intermittent fever. Coincident with the chill there is a rise of temperature. The thermometer shows from three to four degrees Fahrenheit of fever during the first twelve hours, rapidly rising until the temperature reaches from 103° to 105° F. or even more. Then there is a period during which the temperature is maintained with slight variations until from the fifth to the eighth day, when a crisis occurs and the temperature falls abruptly, until within a few hours it becomes normal.

Cough is an early symptom, but it is repressed as much as possible to avoid the severe pain it causes. The expectoration is apt to be frothy at first, and mixed with florid blood; later it becomes viscid and very tenacious, so that it is spat out with difficulty and adheres like thick mucilage to the vessel containing it. Its color at this stage varies in different cases. It may be a light yellow, a pale green, or a chocolate-brown, or a mixture of these colors. It is often likened to prune juice. Sputa of this character may be considered pathognomonic of this disease. As resolution progresses the expectoration becomes less colored, less sticky in consistence, and more catarrhal in its character, and the quantity gradually diminishes until it ceases altogether.

The respirations are early increased in frequency, and this quite out of proportion to the increase in pulse rate and temperature. With a pulse of not more than 90 the respirations will number 30 or more to the minute. In nearly every severe case there will be a time when the respirations will go up to 40 or 50, and they not infrequently reach 60 or more per minute, when the consolidation is extensive or pulmonary œdema takes place. The pulse is usually full and strong in the early stages, numbering from 90 to 100 when the temperature is 103.5° to 104°, and becoming weaker and more frequent as the disease advances. When the respiration is greatly embarrassed the pulse is apt to be small and creeping, unless affected by stimulants.

The skin is hot and dry at first, later there is a tendency to perspiration which may be profuse. The face is pale, with often a dusky red patch on either cheek. The lips are inclined to a bluish hue in proportion to the degree of pulmonary implication. They are often the seat of an herpetic eruption.

After the first forty-eight hours the chlorides in the urine are greatly diminished in quantity, or entirely absent. In severe cases a moderate degree of albuminuria is common during the height of the fever.

The physical signs begin to be appreciable as a rule within from

twelve to twenty-four hours after the initial chill. Usually the first to be noticed is a fine crepitant râle, heard only with inspiration, though in some cases this is preceded by a diminished clearness of the respiratory murmur. Dulness on percussion succeeds, increasing in intensity as the consolidation becomes more complete. Ultimately the respiratory murmur is wholly replaced in the affected area by a peculiar whiffing sound heard most distinctly towards the close of expiration, the so-called tubular breathing. If the pleura is involved there may be a rubbing or creaking sound in addition. There are increased vocal resonance and vocal fremitus.

As resolution progresses the auscultatory signs reappear and again disappear in the reverse order of their original sequence. At the crisis, while the temperature falls and the pulse and respiration become less frequent, there is no immediate change in the physical signs, showing that the condition of the affected area remains the same.

In a large proportion of cases of pneumonia there is decided leucocytosis, the white cells numbering 20,000, 30,000, 40,000 or more to the cubic millimetre.

This being a general picture of the disease we will examine its features more in detail, noting as we proceed the variations more or less frequently observed from the typical course of the affection.

Prodromes.—In about twenty-five to thirty per cent. of the cases of pneumonia there are prodromes. In the aged the proportion is higher, reaching to sixty per cent.[1] There may be for several days before the seizure a general feeling of malaise, headache, loss of appetite, dull pains in limbs and back, perhaps diarrhœa or epistaxis. The skin may have a sallow appearance suggesting slight jaundice. Chilly sensations alternating with flashes of heat may be experienced.

These symptoms, leading up to the fully developed attack, are accepted as a part of the seizure, an initial stage of the pneumonia depending upon the specific infection.

Andral[2] relates a case in which the general symptoms of headache, debility, dulness of the intellectual faculties, flushed face, injected eyes, and a frequent pulse appeared at least six days before the physical signs could be detected.

The Initial Pain.—This is usually sudden in its onset. Not infrequently the patient is awakened in the night by a sharp pain in the chest, much aggravated by every movement of respiration. This pain may be felt in any part of the thorax, but is most often referred to the region of the nipple on the affected side. Instinctively the respiratory movements are restricted in amplitude, and to compensate for this become more frequent. It will be observed that the

sound side of the chest expands more than its fellow. There are cases, however, in which there is only a dull heavy aching, and sometimes no complaint of pain whatever is made. When the pain is sharp it is no doubt due to accompanying pleuritis, while the dull aching has its seat in the pulmonary parenchyma, the pleura not being involved, and the dull pain not being masked by the more severe.

In some instances the pain is referred to a point entirely outside of the chest. Thus, I recall a case in which the pain, which was very acute, was felt in the abdomen, and attention was thus diverted for a time from the real seat and nature of the disease. In many cases the pain is felt with great intensity some hours or even a day or two before there is any considerable rise in temperature or before the physical signs can be recognized. That the pleura should be thus irritated before there are any other symptoms or signs of pleurisy, and while the pneumonic process is still undeveloped, would seem to indicate a special susceptibility of the serous membrane to the very early local action of the toxin. It has been suggested that the pain was due to the stretching of the inflamed pleura by the swelling of the subjacent lung,[3] but this is at variance with the facts above mentioned.

The duration of the pain does not often exceed two or three days. As consolidation becomes more complete the movements of the lung nearly cease, and the friction of the pleural surfaces upon each other being less, the pain is diminished in proportion.

The Chill.—This is not uniformly present. It was absent in 35 per cent. of 223 cases observed at the Presbyterian Hospital. Elsner found it absent in 30 out of 150 cases.[4] It marks the moment at which the system feels the brunt of the infection, and from what we now know of the infectious diseases as a class, its occurrence alone would raise the presumption that pneumonia was such a disease. It varies greatly both in intensity and duration; in one case scarcely attracting the notice of the patient, and in another occurring as a severe rigor lasting for an hour or more, and leaving after it a sense of profound depression. Its severity generally bears a relation to the severity of the infection as expressed by the effect upon the nervous system rather than upon the temperature, and it has a prognostic significance which will be dwelt upon in another section.

It is sometimes, though not often, repeated when a fresh invasion of lung occurs. Usually the cases in which it is absent are mild, or they have the type of bronchopneumonia rather than of the distinctively croupous form.

The relation of the chill to the local condition is not clear. By

many it is considered as marking a general infection of which the lung changes are a subsequent expression. In proof of this view it is put forward that the physical signs are often not developed until some time has elapsed after the chill. Indeed, Syers[5] reports five cases of pneumonia entirely without physical signs of lung consolidation. In each case the illness began suddenly; the temperature was high and fell by crisis; there was labial herpes; and the pulse-respiration ratio was typically that of pneumonia. Still no evidence of lung consolidation was detected in the physical examinations, which were repeated and most thorough. Now while such cases would seem to support the view that pneumonia is primarily a general infection with a secondary local lesion of varying intensity and importance, or which may remain absent altogether, it seems impossible from a careful consideration of all the phenomena to resist the conviction that the disease *begins* in the lungs.

The evidence to the contrary is based on the general assumption that there is no disease in the lungs unless, and until, there are physical signs indicating its presence. But a moment's reflection will show that as the local disease causes the signs, it must *precede* their appearance, and that it must progress to a certain extent before it can manifest itself in a way to be appreciated through all the intervening tissues by the coarse and insensitive methods of auscultation and percussion. That bacteria are developed to a considerable extent during this time, and are actively engaged in the production of toxin, is *a priori* a reasonable inference from the toxæmia which is already present. If we reject this inference we must fall back upon the assumption that some other form of toxin from a microorganism in some other situation exists first, and in some unexplained way ultimately induces the growth of the specific organism in the lungs. Such an assumption is unreasonable in itself, and requires more for its support than the mere absence for a time of the physical signs. Moreover, we find that when rigors occur in other infective diseases, they often appear before there is any local manifestation at all commensurate with the general disturbance. This is especially true of purulent infection. The chill generally precedes any palpable local change, and its appearance is often the first indication that a pus focus is about to develop. Yet we must believe that the initial step is a local infection which even at its inception, so far as we can distinguish, is competent to poison the general system. Just how much toxic material has to be taken up in order to provoke an explosion we do not know, but there is nothing in analogy to forbid the inference that, in pneumonia, a local process going on in the air cells may furnish enough toxin to excite a general reaction without giving rise as yet

to recognizable physical signs. Besides, under the title of prodromes certain symptoms have been mentioned which in a considerable proportion of the cases *precede the chill.* Granting them to be a part of the disease, we have to admit that there is toxin in the blood at a very early stage, often as long as two or three or more days before the physical signs begin to be discoverable. But if there is toxin in the blood, there must be germs somewhere, and where if not in the lung? Hence the inference already drawn seems to be inevitable.

In this connection it is to be noted that different specimens of pneumococci produce toxins differing enormously in virulence, so that in one case a comparatively limited local action may give rise to an intense general infection, while in another case a much greater accumulation of cocci in the lung may have a mild infection as the result.

The Pulse.—In sthenic cases the pulse is at first full, bounding, and incompressible; such a pulse as in former times was held to demand blood-letting. Its frequency bears about the normal relation to the temperature, but less than the normal relation to the respiration. As the disease progresses the pulse tends to increase in frequency and to become less firm. When the pulmonary obstruction is considerable and the blood current is retarded in the lungs the arterial system is left but partly filled and the pulse becomes small and thready. Under these conditions it is often observed to fluctuate in strength with inspiration and expiration, being feebler when the blood is aspirated towards the thorax by the expansion of the chest, and stronger when the contraction of the latter is added to the force of the cardiac systole.

As a rule the pulse decreases in frequency with the fall of the temperature at the crisis. But this is not always so, and a frequent pulse with a low temperature is an association of serious import. It indicates that the system has become deeply infected, and the heart muscle proportionately weakened. In an adult a pulse as high as 120, if maintained from day to day, may well cause serious apprehension. On the other hand, especially in elderly persons, there may be little or no increase in the frequency of the pulse. In young children it often reaches a very high figure, which may even be difficult to count, and yet the danger is not proportionately greater. In fact the pulse is subject to so great variations in sympathy with the disturbance of the nervous system that its indications taken alone are extremely unreliable.

The *respiration* early assumes a frequency which is very characteristic, and is sufficient of itself to excite a suspicion of the nature

of the disease. This increased frequency is due to several causes. Probably there is from the very beginning a specific irritation which is felt in the affected territory in the lung and which excites to greater functional activity.

Hughlings Jackson[6] mentions a case in which the intercostal muscles acted in voluntary, but not in involuntary, respiration. This was one of several cases of pneumonia in which the knee-jerk was absent.

Such cases serve to show the profound effect which the toxin is capable of exerting upon the nervous system, and which extending to the respiratory centre would suggest a partial explanation of the great rapidity of respiration while as yet the respiratory surface is scarcely diminished. In confirmation of this, Washbourn found that mice injected with Fränkel's pneumococcus suffered from dyspnœa even in the absence of pneumonia.

Next, the pain which is felt in most cases tends to prevent a full expansion of the thorax, and there is consequently an effort to make up by frequency of breathing what is lost in amplitude. This is evidenced by the superficial character of the respiration, and the fact that even before the expansion of the lung is lessened by solidification the affected side of the chest may often be seen to move less freely than the other. Then comes the influence of the fever, which of itself should give about one additional respiration for each increase of four beats of the pulse, or one degree Fahrenheit of temperature. Lastly there is added, as congestion and consolidation become factors in the case, the effect of reduced respiratory surface.

These causes combined result in a frequency of the respiration out of all proportion to the pulse and temperature. Thus seventeen cases of pneumonia observed with reference to this point at the Presbyterian Hospital gave as the average maximum of temperature, pulse, and respiration, 104.4°, 131, and 57 respectively. It will be noticed that the usual ratio of the pulse to the temperature, viz., increase of ten beats for each degree of rise, is very closely maintained, while the usual ratio of one respiration to four pulse beats is changed to about one to two and two-thirds.

At the crisis the respiration falls with the pulse and temperature, but not in equal degree, running usually between 20 and 25, while the temperature is normal or subnormal, and the pulse about 80. This fall of the respiration without a corresponding change in the available breathing surface is often cited as a proof that the pulmonary conditions have very little share in making up the gravity of the case. But, it is not to be overlooked that after the crisis the respiration maintains its comparatively low rate only in the

absence of all muscular effort, and when there is no accession of temperature. Should the patient attempt any exertion, or should the temperature rise again from any cause an immediate quickening of the respiration to a disproportionate degree would show the crippled condition of the lung. There is normally a wide margin of respiratory surface which can be drawn upon without greatly disturbing the breathing. But, with this margin exhausted the slightest tax upon the respiration either by muscular effort or by rise of temperature makes itself felt at once.

Pregnancy, rachitis, Pott's disease, pulmonary emphysema, and all conditions that interfere mechanically with the movements of respiration, add to the dyspnœa, and must be taken into consideration in estimating the degree to which the lungs are affected by the pneumonia itself.

Grisolle insists upon the distinction between real and apparent dyspnœa in pneumonia. The nervous patient, tormented by the stitch that limits the excursion of the ribs, and by an incessant cough will breathe 75 to 80 times per minute. Yet he is really less asphyxiated than the prostrated cyanotic patient who breathes only 24 to 28 times in the same period. The prognosis is determined more by the peripheral cyanosis, the distention of the jugulars, and the state of the pulse and heart than by the apparent dyspnœa.[7]

In pneumonia in the aged, which, however, is apt not to be strictly lobar or croupous, this frequency of respiration together with a moderate degree of fever is often almost the only evidence of the serious character of the attack, and is sufficient to establish the diagnosis in advance of the appearance of the physical signs, which latter are often delayed or imperfectly manifested.

Very frequently the respiration is interspersed with grunting sounds at intervals or perhaps with every expiration. This is most marked during the stage when the pleurisy is at its height, and is usually associated with a more or less soporous condition, the sound ceasing when the patient is aroused.

In cases in which the respiration is labored the alæ of the nose will be observed to expand with each inspiration. This is an automatic movement, and indicates that the respiratory centre is receiving an unusual stimulus. As a prognostic sign it has no special value.

The *temperature* begins to rise from the moment of the attack, and increases with slight fluctuations until the maximum is reached. In cases that pass the crisis the highest point is usually a few hours before the decided fall takes place, the temperature often declining a degree or so, to rise again before the final drop. When death occurs

before the crisis the highest point often immediately precedes dissolution, when the thermometer may indicate 107°, 108°, or even 109°.

Very high temperatures, however, may be recovered from. Francis Hawkins* gives a case of hyperpyrexia with double lobar pneumonia, in which, upon the fifth day of the disease, the temperature rose to 108.4° F. (42.4° C.) as recorded by two different thermometers. The temperature fell by lysis, and became normal on the twenty-ninth day after admission. Patient discharged recovered. The treatment was cold sponging and packing with iced water.

When defervescence occurs by crisis, which is usually from the fifth to the eighth day, the temperature falls within a few hours almost or quite to normal. This is apt to occur during the night, and it often happens that the patient is left at the evening visit with no sign of an approaching decline in temperature, yet the next morning is found in an almost afebrile condition.

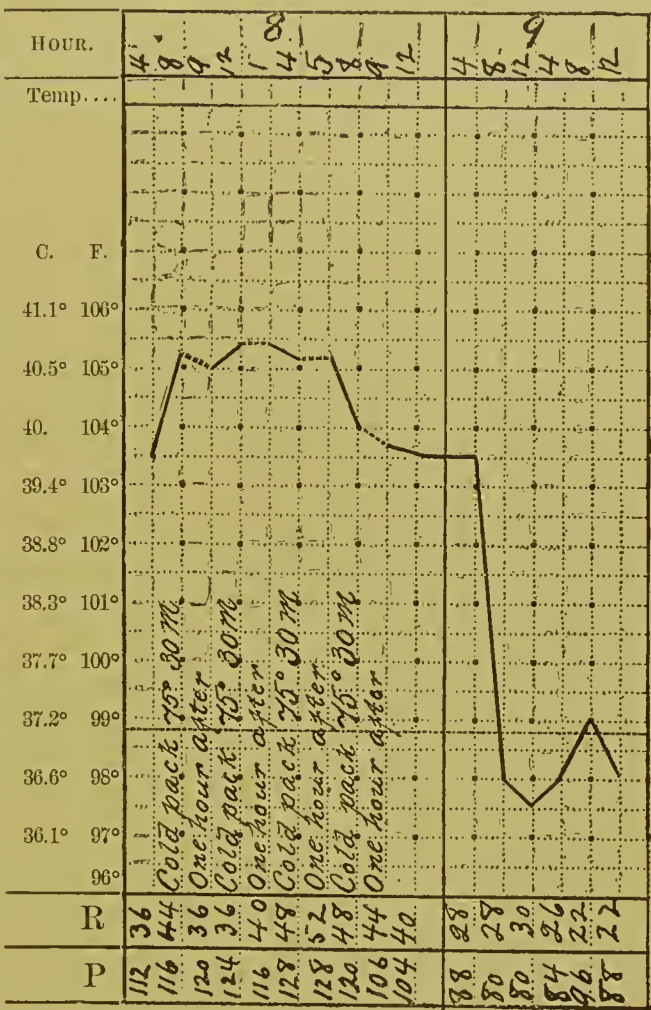

CHART No. 1.—Defervescence by Crisis.

The accompanying chart (No. 1) is of a case admitted on the eighth day of the disease. Pack at 75° F. repeated every four hours produced very little effect, but at the crisis on the ninth day the temperature fell $5\frac{1}{2}$° F. in four hours.

A day or two before the actual crisis there may occur a sudden and considerable drop of temperature, followed promptly by a rise to its former height. This is known as pseudo-crisis. On the other hand, the crisis may be preceded by a brief but marked accession of temperature, the so-called critical perturbation.

An increase of temperature following a decline suggests the involvement of a fresh portion of lung, though it may be due to other causes.

As will be seen later under the head of Prognosis, the severity of the attack is not necessarily in proportion to the temperature; indeed, the greatest danger may be present when the thermometer shows but a moderate rise. Especially in the aged, it is possible for the attack to be afebrile throughout, and to go on to a fatal termination without rise of temperature.

It is to be borne in mind that the temperature of the surface may be but little increased, while that of the interior of the body is alarmingly high. Hence the rectal temperature may be greatly in excess of that observed in the axilla or in the mouth. This is not seldom the case in elderly persons, in whom the peripheral circulation is sluggish. It is also occasionally the result of extreme intensity of the initial infection. Especially in children this high internal temperature may coincide with coldness of the extremities.

At the crisis the face becomes paler and calmer, restlessness and delirium disappear, the skin becomes moist, or there may be profuse sweating, and there is a tendency to sleep. An attack of diarrhœa at this time is not rare. The temperature may fall in from twelve to eighteen hours to 98° or 97° F., but may rise again on the following day to 99° or 100°.

Fowler gives the following as the days of crisis in the order of their frequency: "22 per cent. on the seventh day; 16 per cent. on the fifth day; 12 per cent. each on the sixth and eighth days; and 10 per cent. on the ninth day."

Instead of a complete crisis there may be a considerable and rapid decline of temperature, followed by a rise, and this succeeded in turn by a gradual lysis. Again, there may be a complete well-marked crisis, but the lung remains solid; there is renewed pyrexia and the case goes on to a fatal termination.

In a considerable proportion of cases there is no such sudden fall of temperature as constitutes a crisis, but the temperature, while fluctuating more or less, gradually becomes lower until the normal line is reached. This defervescence by lysis may be complete at any time between the third and the fifteenth or twentieth day (see chart No. 2).

The *cough* is seldom a marked feature. It is accompanied by severe pain in most cases, due to accompanying pleuritis, and for this reason is superficial and catchy. Usually it begins within the first few hours, or in some instances it precedes the distinctive symptoms of the attack. Sometimes, particularly in persons past middle life, it

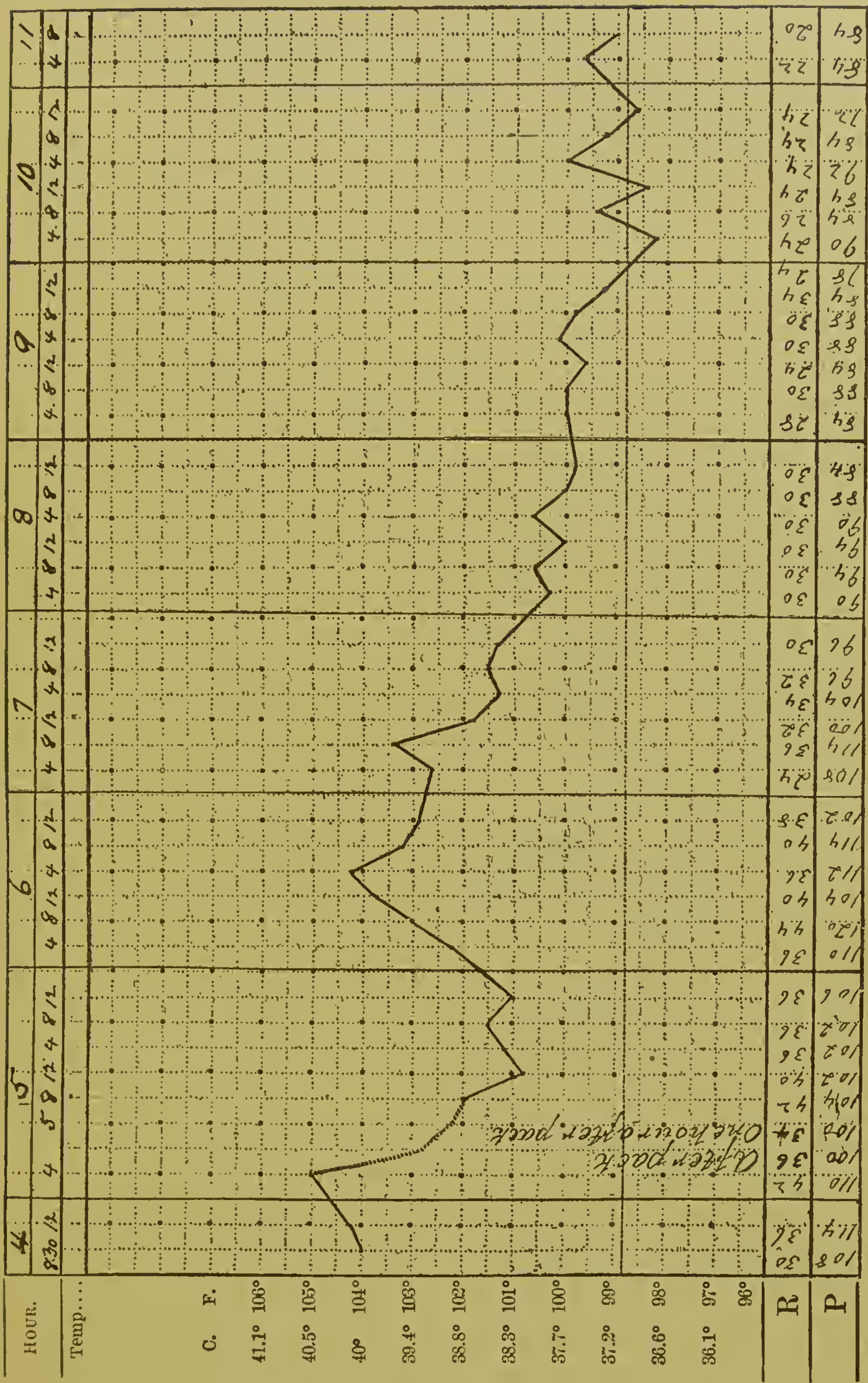

CHART No. 2.—Defervescence by Lysis.

is entirely absent. Severe cough occurring in paroxysms shows that the bronchial surface is involved. Such a cough is usually limited to the early stage of the attack. While it lasts it is the source of considerable distress from the pleuritic pain excited by it.

The *expectoration* is at first frothy and tinged with blood. Occasionally it is almost pure blood. Later it becomes more dense and takes on a yellow, or brownish, or rusty color—according to the amount of blood it contains. The color is not often uniform, but more or less marbled from the aggregation of differently stained masses, varying in color from dark reddish-brown to pinkish or amber, or a greenish tint. With all these colors there is, however, a vitreous, semitranslucent appearance, which is not lost until the abundant admixture of leucocytes at a later stage renders the expectoration opaque. The quantity is not great, seldom exceeding two or three ounces in twenty-four hours. The expectorated material is composed of mucus mixed with leucocytes, red blood cells, epithelia (both columnar and pavement), fibrinous casts of the air cells, formerly described as pneumonic globules, and occasional casts of the bronchioles. Curschmann's spirals are sometimes found in the sputum, but their presence has no diagnostic significance.

The sputum abounds in microorganisms, especially the diplococcus lanceolatus, which, however, diminish rapidly after the crisis. Chemically, it is found to contain a large amount of sodium chloride, while the alkaline phosphates are absent. The extreme adhesiveness of the expectoration has been already referred to. Owing to this it is difficult to eject it from the mouth, as it adheres to the tongue and teeth, often requiring the aid of a handkerchief for its removal.

Later it assumes a more creamy appearance and becomes somewhat less tenacious. At this stage it contains a larger proportion of leucocytes, many of them in a state of fatty degeneration.

Occasionally, instead of this thick sticky material we find a thin fluid deeply stained with a dark coloring-matter derived from the blood. This so-called prune-juice expectoration is supposed to denote a specially unfavorable condition. Probably it depends upon a serous exudation into the air passages, and indicates that the blood is less rich in fibrin than in cases yielding the tenacious sputum.

Now and then we meet with a case of pneumonia in which there is no expectoration from beginning to end. In these cases the exudate is removed by absorption alone. The process of freeing the lung and restoring its permeability is not materially longer than when a part of the effused material is coughed up. Indeed, when we consider the large amount of material to be removed, it is evident that the quantity represented by the expectoration must count for very

little in the process. In fact, the bulk of the expectorated material in any case is furnished by the coincident bronchitis.

An expectoration such as is described above is fairly pathognomonic. In no other affection do we have these sticky, tenacious, variously colored sputa. In bronchitis occasional isolated masses somewhat resembling them in character may be found, intermixed with watery and frothy material, but they lack the adhesive quality by which the whole contents of the cup are bound together, and they assume rather more of a nummular form.

The *posture* in pneumonia is indicative of a chest affection. The patient lies at first on the back, as rendering the respiration less painful; but as consolidation progresses, the increased weight of the affected lung makes the decubitus on that side more comfortable than any other position, as there is less pressure upon the sound lung, and the breathing is therefore easier. There is not the frequent change of posture so common in simple pleurisy; the patient having found the position that suits him the best, is likely to maintain it pretty steadily. Orthopnœa is rarely observed, unless there is fluid in the pleural cavity or a considerable degree of pulmonary œdema.

The *face* is apt to have a more or less dusky hue, in proportion to the respiratory involvement, and the lips are pale with a bluish tint in most of the severe cases. The countenance has a pained and anxious expression and the aspect is that of a person seriously ill. There is often evidence of great weakness and a tendency to slip down in the bed, which may be quite as marked as in typhoid fever. This, however, is far from being a constant feature, some persons retaining a remarkable degree of strength throughout the whole attack. The difference in this respect will be referred to again in another connection.

The Blood.—From the outset the number of leucocytes in the blood is usually considerably increased, reaching sometimes as high as 40,000 to 60,000 per cubic millimetre. According to Stienon,[9] during the pyrexia the polynuclear cells are very abundant and the eosinophiles very rare. After the crisis the former diminish, and the latter increase. The subject of leucocytosis will be further considered under the head of Prognosis.

It has long been known that in pneumonia the proportion of fibrin in the blood is greatly increased. This increase may amount to as much as two hundred and fifty per cent.

The Urine.—The absence of chlorides from the urine is a pretty constant condition after the first two or three days. The quantity becomes less as the process of consolidation advances, and, as the

exudate in the lung is enormously rich in chlorides, it seems a fair inference that they escape into the alveoli in place of being excreted by the kidneys. This inference is strengthened by the fact that during the absorption of the exudate the quantity of chlorides thrown out by the kidneys is abnormally great. In obscure cases this disappearance, partial or complete, of the chlorides from the urine may have considerable diagnostic value, although it may occur in other diseases.

F. Pick [10] calls attention to a change in the urine in pneumonia not described hitherto. In from twenty-four to forty-eight hours after the crisis there is a decided decrease of acidity, the urine becoming neutral or alkaline. This condition continues for from twenty-four to thirty-six hours and then the acidity returns.

The phenomenon is of pretty constant occurrence, Pick having observed it in thirty-one out of thirty-eight cases. He ascribes it to the absorption of the exudate, which is rich in sodium. It may be due, however, to sodium being excreted in the urine as bicarbonate, which under normal conditions would have been neutralized by pneumic acid in passing through the lungs (see page 44).

In a considerable proportion of cases of pneumonia albumin is found in the urine. Owen found it in all but four of twenty-six cases.[11] The amount bears some relation to the severity of the case. The albuminuria is probably the result of several contributing causes. The infection itself, like other acute infections, has a tendency to produce this result, the pneumotoxin probably irritating the kidneys as so many other toxins do. Secondly, the interference with the pulmonary circulation results in more or less tension of the venous system, congesting the kidneys; and lastly, the imperfect metabolism consequent upon incomplete hæmatosis leaves material in the blood to be thrown out by the kidneys, which material normally would be destroyed by oxidation.

Besides albumin, blood and fibrinous casts of the uriniferous tubes are occasionally found in the urine.

According to Sternberg,[12] secondary infection of the kidneys by the micrococcus pneumoniæ crouposæ is probably not infrequent. The micrococcus is not ordinarily found in the blood in pneumonia, though sometimes present in small numbers. Fraenkel and Reiche (1894) found this micrococcus in the kidneys in twenty-two out of twenty-four autopsies upon cases of pneumonia, and had a bacteriological examination of the urine been made during life, it is probable that the pneumococcus would have been found there.

In a certain number of cases, undoubtedly, the kidney disease is due to the presence of the pneumococcus itself in the kidney. Such

a condition could be demonstrated during life only by finding the organism in the urine in a case presenting symptoms of renal irritation.

The most recent observations go to show that cases in which secondary infection by the coccus itself occurs in organs other than the lungs usually prove fatal, and it is probable that these secondary infections very often determine the issue of the primary disease. The albuminuria in the simple form begins to clear up after defervescence, except in cases in which the respiratory embarrassment continues after the fall of the temperature.

Associated with the albumin hæmoglobin may appear in the urine. Nash[13] mentions a case in a girl of sixteen ill four days with pneumonia. The crisis occurred on the seventh day, after which no more coloring-matter or albumin could be detected.

An early appearance of albumin in the urine, before the pulmonary circulation is materially obstructed, may be interpreted as indicating a high degree of infection, and therefore as likely to be followed by severe depression. Usually its first appearance is when the disease is at its height.

The prognostic significance of albuminuria in this affection is important in proportion to the degree of renal implication present. This is judged of by the quantity of albumin on the one hand and the associated symptoms on the other. A large amount of albumin in a scanty urine containing epithelial casts and perhaps blood discs, the fever at the same time being high, the stomach irritable, and the mental faculties clouded, creates a presumption that organic change is present in the kidney. Such change alone constitutes a grave element in the prognosis, but when we consider that lying back of it there is likely to be an infection of the kidney by the organism itself as well as by the toxin, and that in this case the germ being in the blood, other organs also will be involved, it gives an extremely serious aspect to the case. Should an examination of the blood show the presence of active pneumococci, the prognosis would be almost hopeless. Sturges and Coupland found that of twenty-seven cases in which albuminuria of all grades was present five were fatal, while of seventy-one without albuminuria all but two recovered. From these figures it would seem that pneumonia with albuminuria is more than six times as fatal as without it. It would be wrong, however, to infer that such an increase of mortality is due to the kidney affection by itself. We should rather note the fact that this affection is prone to appear in cases that are otherwise bad, and more likely, therefore, to prove fatal.

Regarded as a complication, acute parenchymatous nephritis is

not uncommon. Osler[14] found marked interstitial changes in the kidneys in twenty-five per cent. of the cases that came to autopsy at the Montreal General Hospital. It is very rare that it is the foundation of permanent disease.

A further effect of the disease upon the renal function is a remarkable diminution of the toxicity of the urine. According to researches by Roger and Gaume,[15] the toxicity is only one-fourth of the normal during the pyrexia, but rises to the normal or beyond it at the crisis.

It would seem from this that either the disease so acts upon the chemical processes that the usual amount of toxins is not formed, or that the kidneys fail to eliminate the toxins in full measure from the blood. While it is not at all impossible that the latter is the case in some degree, and that the retained toxins may play a part in producing the general condition, still as the lessened toxicity is not necessarily accompanied by evidence of kidney implication it seems more probable that it depends upon a fault in the chemical processes by which the toxic material is formed.

Throughout the febrile stage the quantity of urea is abnormally great, the urine is scanty, and the specific gravity is excessive.

After the crisis the urine becomes more abundant, but the excess of urea persists for some time, and may be greater even than when the pyrexia was present. This is probably due to the formation of urea from the exudate absorbed from the lung. According to Herter, the uric acid also is greatly increased.

Delirium.—The mental condition is more or less disturbed in a majority of cases. As the pyrexia increases delirium is pretty frequently observed. It may take the form of simple incoherence of speech, or it may be of the active, busy sort. Occurring early and in persons who naturally show a tendency to cerebral derangement in the presence of fever, it may have but little significance. Even the moderate pyrexia attending a severe cold will sometimes cause a passing delirium in such patients, and if attacked with pneumonia they are likely from the outset to appear more ill than they really are, so far at least as the mental condition indicates. But in other cases the delirium is a part of the general nervous perturbation to which the infection gives rise, and it then points to a condition of considerable gravity. For some reason not yet explained, it is more prone to occur in apical pneumonia than when the lower lobes are involved, though this is denied by some observers.

Old persons are especially liable to a quiet delirium resembling that of typhoid fever.

Persons delirious from pneumonia require special watchfulness on the part of nurses and attendants. Occasionally the patient be-

comes maniacal, and seeks to escape from imaginary enemies. Thus a young man, not alcoholic, in the service of the writer in the New York Presbyterian Hospital, during a momentary absence of the attendant, dashed across the ward and through the sash of a closed window, and fell from the second story to the ground. He recovered from his pneumonia and from the injuries sustained from the fall. In alcoholics this sudden frenzy is of frequent occurrence.

The delirium is not always proportioned to, or dependent upon, the temperature. It may be present when the pyrexia is very moderate. When this is the case it is of evil omen, as it indicates cerebral exhaustion. It may be a question whether the brain symptoms in a given case are the result merely of disturbed cerebral nutrition as in many other forms of disease, or whether they depend upon the direct local action of the microbe. The frequency with which the pneumococcus is found in the fluid of meningitis, even when pneumonia is not present, shows that it has a special predilection for that locality, and it is perhaps more frequently present than we are in the habit of admitting. If autopsies in pneumonia more generally included the cranial cavity, it is probable that more cases of meningitis would be discovered; its distinctive clinical features being masked by those of the primary disease.

When the aëration of the blood is seriously interfered with, we have in this condition alone a sufficient cause for some degree of mental disturbance, which shows itself more particularly in somnolence or coma.

According to Potain,[16] of Paris, the delirium of pneumonia is the result of varied conditions of the cerebrum; ranging from simple excitement, through the meningitis state, to true meningitis. Following the excited stage there is a period of quiet that deepens into coma, at times associated with signs of compression of the basilar cranial nerves. The meningitis may be apoplectic in character.

Aside from the occurrence of delirium there are other evidences of nervous implication. The most striking, perhaps, is the extreme *prostration* that marks certain cases even in the early stage. It is not uncommon that a patient is stricken down in a way that at once suggests the agency of a powerful infection. His strength leaves him, he takes immediately to his bed, his limbs shake, his tongue is tremulous, his head and bones ache, he is nauseated and perhaps vomits. All this is in addition to the chill and to the stitch, and seems at a stroke to deprive the patient of half his vitality. It is in striking contrast to the comparatively slight impression upon the nervous system which is often noted in cases in which the temperature may be higher and the pulmonary condition much more serious.

Sleeplessness is another condition not at all uncommon. Sometimes for nights and days there is no sleep, unless the patient is overwhelmed with hypnotics. This condition should always suggest a careful inquiry into the previous habits of the patient, for while it is by no means confined to those with alcoholic antecedents, it is much more frequent in such persons, and in the absence of delirium the key to the problem might be overlooked. In subjects not alcoholic, the condition seems to be one of cerebral irritation at first, and later, perhaps, of cerebral exhaustion.

In children often, and very rarely in adults, *convulsions* take the place of the initial chill. As the disease progresses, and particularly in cases in which hæmatosis is seriously interfered with, somnolence, deepening into *coma*, is a very frequent condition. As this tends to favor the occurrence or aggravation of hypostatic congestion, frequent efforts should be made to arouse the patient that he may be excited to more vigorous respiration. Life may hinge upon the observance of this precaution at a critical juncture. Sponging the face, neck, and between the shoulders with ice water is an efficient means of recalling the patient to consciousness under these conditions.

Causes of Death.—In fatal cases death may occur in a variety of ways. First, there are cases in which the patient is overwhelmed by the intense virulence of the infection, death occurring within from thirty-six to forty-eight hours after the chill. It would seem as if all the vital functions were overpowered by the toxæmia. There is extreme muscular and nervous prostration, the heart's action becomes rapid and feeble, digestion is suspended, the kidneys act imperfectly, delirium and coma supervene, and death occurs from acute asthenia.

In other cases death is caused by exhaustion of the right heart. The muscle tires out from overwork, being enfeebled already by the action of the poison. Later, dilatation takes place, perhaps to the extent of producing incompetence of the tricuspid valves. Finally, it becomes so overdistended that it cannot recover itself and asystole results.

Still another cause of death is loss of respiratory surface. This is rarely the result of simple pneumonic consolidation, but there is added to this congestion an œdema of other portions of the lung. In these cases the lungs fill up more and more; the breathing becomes more and more rapid and superficial; and death by asphyxia takes place.

Plicque[17] lays much stress upon this mode of death, declaring that nine patients succumb to it for one dying from the infection.

In a considerable proportion of cases death comes from exhaustion of the vital powers, after a protracted and intense struggle which

the system is unable longer to continue. This is common in feeble and old persons, and is marked by a gradual giving out of the forces. It usually does not occur until after the febrile period.

Lastly, death may be caused by one or more of the many complications to be described hereafter.

In addition to the foregoing, sudden death may occur at any stage of pneumonia, with no previous warning.

As remarked by Wells,[17] cases of this kind caused by heart clot, paralysis of the heart, and apoplexy may be readily explained, but there are cases in which no gross anatomical lesion can be found, and which with our present knowledge cannot be accounted for. Wells[18] quotes a number of such cases. The essay referred to contains a great amount of material that cannot be presented here, but which is extremely interesting.

Physical Signs.

Usually, even before there is notable dulness on percussion, and sometimes within three or four hours after the beginning of the attack, we have a fine crepitant râle over the seat of the lesion. This is a sign commonly regarded as peculiar to pneumonia. It is heard only during inspiration, and often is confined to the last third of the inspiratory act. It has been likened to the crackling of salt thrown upon a heated surface, or to the sound produced by rubbing a lock of hair between the thumb and finger. A still more accurate comparison is with the crackling of a static electric machine when the poles are almost in contact. It is supposed to be produced by the bursting of minute air bubbles in the bronchioles or alveoli. It is not to be confounded with the subcrepitant râle, which is coarser, and is heard in expiration as well as inspiration. The crepitant râle ceases when consolidation takes place, the exuded material then occupying the alveoli and excluding the air. The crepitant râle is absent in a small proportion of cases. It sometimes disappears for a time and then returns, to disappear finally as the solidification becomes complete.[19] This sign is accurately limited to the affected portion of the lung, not being heard outside of the pneumonic area, although not always present in all parts embraced within that area. Indeed, in most cases we fail to find it over a large surface at any one time, though repeated examinations will reveal its presence at different points. This is due to its dependence upon transient conditions that vary within narrow limits with the changes going on in the lung, and to the crepitation not being a sound of sufficient intensity to be heard at any distance from the point at which it is produced.

It may be reproduced when the exudate begins to resolve. Re-

curring during resolution it is known as the *crepitus redux* or *râle redux.* It then is coarser than the true crepitant râle, and partakes rather of the character of the subcrepitant.

As consolidation proceeds the crepitant râle is replaced by a new sound, bronchial or tubular breathing. The French call this the *pneumonic souffle.* It is a high-pitched, whiff-like sound, and may be closely imitated by stroking the coat sleeve lightly with the tips of the fingers. Often it is heard only in expiration, during which the current of air is more rapid than during the slower movement of inspiration. It is produced by the passage of air through the finer tubes, the vibrations being conducted with especial clearness by the solid tissue of the surrounding lung. It simply indicates consolidation, and therefore is not distinctive of pneumonia. At first it merely modifies the vesicular murmur, giving rise to *bronchovesicular* respiration, but as the alveoli become more completely filled it excludes vesicular respiration completely in expiration, and imparts a decidedly bronchial character to the inspiratory sound, which sound is at the same time shortened and incomplete. It is a sound of considerable intensity, and may be transmitted to some little distance beyond the consolidated area, and even over the contiguous portion of the sound lung. In children this is especially the case. When fully developed, bronchial respiration is usually a persistent sign, being found at each examination during the whole period of consolidation. If temporarily absent from a locality where it was formerly found, the absence is due to a transient obstruction of a bronchial tube.

If a considerable area of lung is consolidated and therefore withdrawn from action, a compensatory increase of expansion of the unaffected portion is necessitated, and as a result we have exaggeration of the normal respiratory murmur, the condition known as *puerile* respiration. This may be very marked, not only in the sound parts of the affected lung, but also throughout the other lung as well.

The vocal resonance is modified by the greater density of the medium through which it is conveyed. The sound becomes loud, harsh, and metallic, reminding one of the voice as heard through a telephone. To this sign the term *bronchophony* is applied. In eliciting this sign it is important to cause the patient to speak as much as possible *from the chest.* As this is difficult in the case of women, the vocal signs in them are much less marked and conclusive than in men. Much depends upon the words the patient is required to pronounce. The usual *one, two, three* will illustrate this, the first giving much more decided results than the second and third. It is to be borne in mind that the normal vocal resonance is more pronounced on the right side than on the left. In some cases *pectoriloquy* is developed,

that is, the words spoken are heard as distinct articular speech, when the ear is applied to the chest. Bronchophony is not developed until the second stage, as it depends upon solidification of the lung. In the normal condition the sound vibrations formed in the bronchial tubes are greatly softened, or almost suppressed, by the spongy lung tissue interposed between the tubes and the chest wall. When this tissue becomes solid by the filling up of the air cells, the bronchial sounds are transmitted directly to the surface, and seem to be formed immediately under the ear of the auscultator. This apparent near-

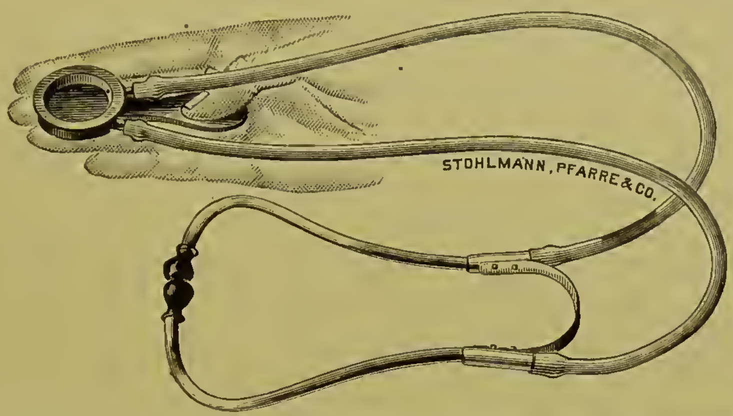

FIG. 1.—Stethoscope for Auscultation of the Posterior Portion of the Chest, the Patient Being in a Recumbent Position.

ness of the sound, which is sometimes almost startling, is quite as characteristic of bronchophony as is the modified character of the sound itself.

Like tubular breathing this sign is merely significant of solidified lung, and therefore does not necessarily indicate the presence of pneumonia. In connection with other signs and symptoms, however, it is of great diagnostic value.

Along with bronchophony goes *increased vocal fremitus.* This may be appreciated by placing the palm upon the chest, or more delicately by pressing lightly with the finger tips in the intercostal spaces. In cases in which there is abundant pleuritic exudation over the pneumonic lung, the fremitus is less exaggerated.

Very often the sounds of the heart are heard over a greatly increased area, being conveyed to a distance by the consolidated lung.

In pneumonia it is often difficult to auscultate the posterior portion of the chest. To turn the patient so as to bring the affected side uppermost will frequently cause extreme respiratory distress; and with a weak heart it is not wise to raise him into a sitting posture. To meet this difficulty I have devised a stethoscope (Fig. 1) that, by pressing down the mattress with the left hand, can be slipped under

the patient on the fingers of the right. The cup of the stethoscope is flat and shallow, in shape like the cover of a pill box; and the rubber tubes instead of coming off from the top, come off from the side at points but little removed from each other. The thickness of the cup is about half an inch. With this instrument the auscultatory signs can be obtained with scarcely any disturbance of the patient.

Very early in the progress of the case a degree of *percussion dulness* is observed. At first it is very slight, and is appreciated only by comparison with the note obtained over the corresponding location on the sound side. But it soon becomes more pronounced, and when the consolidation is fully developed the percussion note is but a shade removed from absolute flatness. Beginning in a portion of the lobe, it spreads usually until the entire lobe is included. Often it is pronounced at first only at a central point, from which the dulness fades away in all directions, but as time goes on the area increases until it accurately represents the contour of the lobe. If a second lobe becomes involved it is rarely by continuity, most commonly by the formation of a second distinct focus.

In some instances, however, the vesicular resonance is replaced by a sound which is more or less tympanitic, *skodaic resonance.* It is high-pitched and wooden in character, as when one taps with the fingers on a table. The contrast is marked with flatness on the one hand, and with the sonorous resonance of pneumothorax on the other. This type of resonance is produced in the bronchial tubes within the consolidated area, the air within these tubes being caused to vibrate by the impulse conveyed to it through the solidified lung, and the vibrations being transmitted in turn through the same medium to the surface. Over the larger bronchi the cracked-pot sound may occasionally be elicited, the shock of the percussion stroke being transmitted in the same manner.

Along with the dulness on percussion, or the peculiar form of tympany, as the case may be, there is a well-marked sense of resistance imparted to the finger over the consolidated area. This will serve to correct any erroneous inference that might be drawn from an unexpectedly resonant percussion note. This sense of resistance is often more appreciable than the actual percussion dulness.

With regard to all these physical signs, however, it is to be borne in mind that when the consolidation begins centrally in the lobe it may not be possible at once to obtain the usual results of auscultation and percussion, the intervening normal lung preventing the abnormal sounds from reaching the ear, and at the same time giving out a clear note on percussion. In such cases we have to depend for a while on the rational symptoms for a diagnosis. But it is not as

a rule more than one or two days before the physical signs begin to be apparent, and in the end we may have them as clearly presented as under the usual conditions. This central beginning with the delayed physical signs is very apt to occur in patients advanced in age, or in whom, from any cause, the vital powers are not active.

In the aged the physical signs lose somewhat of their distinctiveness. There is a tendency to increased resonance on percussion due to the rigidity of the bony framework of the chest, the greater depth of the thorax, and the backward curvature of the spine. The calcification of the rings of the trachea and bronchial tubes makes both the percussion note and the voice sound more sonorous, while it impairs the distinctive character of vesicular breathing, substituting a somewhat bronchial quality. The excess of the bronchial secretion, which is almost physiological in old age, is likely to obscure the crepitant râle, which, in any case, is frequently absent in senile pneumonia.

Auscultation of the Right Heart.—In a considerable proportion, perhaps more than half, of the cases of pneumonia, we have sooner or later to confront what may become a very serious mechanical condition—the overfilling of the right heart and the venous system. This condition has its appropriate signs and symptoms, in speaking of which I shall use to a considerable extent the language of a former communication.[20]

Whenever there is obstruction of the pulmonary circulation, the labor of the right heart is necessarily increased. In proportion to its inability to overcome the obstruction, there will be an accumulation of blood in the venous system. Excess of blood in the veins implies deficiency in the arteries, and hence this class of cases is characterized by an unequal divison of the blood between the venous circulation and the arterial.

This condition has extremely important consequences, especially in acute pulmonary affections. In these we study the pulse with the greatest solicitude to judge how the heart, as we say, is supporting the struggle. But the arterial pulse gives no indication of the immediate peril, for it is not the left heart that is bearing the brunt of the battle. The pulse tells its story only at second-hand. It may be small and weak, but it is chiefly because the left heart does not receive enough blood from the lungs to fill its chambers and to distend the arteries. The trouble is not in a lack of propelling power so much as in deficiency of blood to be propelled.

But if, instead of feeling the radial pulse, we could lay our finger upon the pulmonary artery, we should obtain information vastly more to the point. We should then be able to appreciate the degree of pulmonary obstruction by the fulness of the vessel, and to rate the

power of the right ventricle by the force of the arterial beat. And in the relation of these two factors one to the other is involved the issue of the case. Increasing obstruction with decreasing right-heart power means death; decreasing obstruction with sustained right-heart power gives promise of recovery. It is a question with which the left heart, and therefore the radial pulse, has almost nothing to do. For the peril is not from general exhaustion, as for example in fever, nor from failure of the heart as a whole, as in some cases of infection, but specifically from tiring out of the *right* heart in its effort to unload the venous circulation through the obstructed vessels of the lungs.

Now, while we cannot place our finger upon the pulmonary artery, we can obtain nearly the same information by applying the stethoscope over the pulmonary valve. Owing to anatomical conditions which it is not necessary to describe here, it is entirely practicable to separate the pulmonary valve sounds from the aortic, and by means of auscultation to study the peculiarities of the former as indicating the condition of the pulmonary circulation.

Unfortunately, however, in some cases the valve sound is masked by bronchial râles, so that it may be impossible to appreciate it accurately. But even in the most rapid breathing there are brief intervals during which the practised ear may nearly always gather the required information.

Now, if we note carefully the sound of the pulmonary valve in, for example, a case of pneumonia, we shall find that at the outset, while the right ventricle is still in vigorous action, this sound is especially clear and sharp, indicating a quick and strong recoil of the pulmonary artery following the ventricular systole. This sharp recoil is due to unusual distention of the vessel, and this in turn is due to the resistance which the blood meets in passing through the lungs.

If the case is to terminate favorably, this accentuation of the pulmonary sound will probably continue through the whole course of the disease, becoming less marked as the obstruction in the lung decreases. But in cases of increasing severity and with an unfavorable tendency, a time soon comes when not only this accentuation is lost, but the normal intensity of the valve sound is lessened, the sound becoming weaker and weaker until it ceases to be heard. This means, not that the obstruction has become less, but simply that tho muscular power of the right ventricle has become exhausted with the labor exacted of it. The blood is no longer driven through the artery with sufficient force to distend it, and there is not enough recoil to bring the valve cusps together with an audible sound.

When this point is reached, the end is not far off. The weaken-

ing of the right heart favors still greater pulmonary obstruction, and this in turn adds to the burden of the right ventricle, thus completing the vicious circle. The struggles of the ventricle become feebler and feebler, while the tension within its cavity constantly increases, as the blood presses into it from behind. At last there comes a moment when the overtaxed muscle cannot summon the energy for another contraction, and its action ceases in diastole.

The steps which lead up to this result are in a great degree traceable by symptoms and physical signs. First of all, there are auscultatory and other signs of pulmonary obstruction; then come signs of general venous congestion. The distended right auricle may be traceable by percussion, or even may be seen pulsating at the right of the sternum. An increased area of cardiac dulness extending towards the xiphoid cartilage indicates the repletion of the right ventricle, and in spare subjects the labored beating of this may be felt by pressing the fingers under the costal cartilages. The superficial veins are seen to be unusually prominent, and the liver is enlarged. The spleen also is increased in size, and evidence of intestinal congestion may be afforded by copious diarrhœa.

Proof of passive hyperæmia of the kidneys is found in lessened excretion and in albuminuria. Thus all things combine to indicate a general preponderance of blood in the venous side of the circulation, the result which we should naturally expect from a retardation of the blood in the pulmonary vessels.

Clinical Types.

Bearing in mind that in a very large proportion of the community the potential cause of pneumonia is already present in the pneumococci so often to be found in the air passages, it is easy to understand that a great variety of circumstances may act as exciting causes and determine an attack. Under normal conditions the vital forces are sufficient to protect the individual against the microbic action, but any influence which impairs this defence may open the way to effective invasion. These influences present a great variety, and it has been the custom with some writers to classify pneumonia according to the condition which seems to have given rise to it. Thus, we have bilious pneumonia, grippe pneumonia, malarial pneumonia, typhoid pneumonia, rheumatic pneumonia, traumatic pneumonia, etc., etc. With our present knowledge it is clear that these are not varieties of the disease, but merely designations of the agency by which in any particular case the defences of the system have been broken down and the specific germ afforded an opportunity to act. In some

instances there is a mingling of the phenomena of the exciting cause with those of the induced pneumonia, as when the fever under the influence of malarial infection takes on a remittent type, or the presence of tubercle in the lung complicates the physical signs or changes the typical temperature curve.

But while it does not seem that any useful purpose would be served by adopting such a classification and describing the various forms into which pneumonia may thus be divided, yet the prominent features of the disease vary in different cases, and the variations for the most part group themselves into three divisions, more or less marked, constituting three general types which shade into each other. In a clinical lecture by the writer, published in 1895, and in which these types are described the following passages occur.[21]

"To-day it is generally recognized that pneumonia is a disease of microbic origin, and that while the direct action of the microbe is limited in a greater or less degree to the lungs, the toxin derived from it pervades the entire system.

"The local lesion is not necessarily in proportion to the systemic infection; that is, we may have a very large implication of the lung with comparatively little evidence of general infection, and conversely we may have severe general infection with but little pulmonary implication. And again, without reference to the amount of lung involved, or even to the degree of fever present, we may have the vital forces but little impaired, or we may have the nervous and muscular systems completely overpowered by the intensity of the poison, constituting a condition that might almost be termed malignant.

"Giving to terms already in use a more definite meaning than they have had heretofore, we may call these two classes of cases *sthenic* and *asthenic*. We may also admit a third division, based upon mechanical conditions by which the pulmonary circulation is rendered especially difficult, and to this division the term *obstructive* may be applied. Viewed then from our present standpoint we may recognize three types of cases of pneumonia: sthenic, asthenic, and obstructive.

"It so happens that we have in the wards at this time patients illustrating these three divisions.

"The first case I will show you is that of a man twenty-eight years of age, of previously good health, and temperate in his habits; he is now in the fourth day of the disease. His initial chill, four days ago, was of moderate severity, the pain in the chest was considerable, the temperature rose on the second day to 103.5° F., and his pulse to 105, and on the following day the temperature reached 104.5° F., and his pulse 116. At this time the respirations were 32 per minute.

There is in this case a remarkable absence of the prostration which we see in many cases of pneumonia. The patient, on arriving at the hospital, insisted upon walking from the carriage to the elevator, and from the elevator to his bed in the ward. You will perceive now that when he is asked to sit up for physical examination of the posterior portion of the chest, he rises without any evidence of feebleness; his hands are perfectly steady, and when his tongue is protruded there is no tremor. He is entirely capable, if allowed to do so, of walking about the ward. His mind is perfectly clear. When asked how he feels, the reply is 'first-rate.' On examination, we find that on the right side, with the exception of the space above the fifth rib in front, and above the middle of the scapula behind, there is evidence of consolidation over the whole lung, that is to say, we have dulness on percussion and tubular respiration. Now, in this case, we have a large mass of lung implicated, while at the same time the constitutional symptoms are relatively slight. We are justified, therefore, in considering that in this case the force of the infection is comparatively moderate, and that the local lesion is the more prominent factor. On examining the heart we find that the pulmonary second sound is decidedly accentuated, indicating that there is marked obstruction to the pulmonary circulation on the one hand, and, on the other, a vigorous action of the right side of the heart. The blood is propelled into the pulmonary artery with force, but meeting resistance in the pulmonary circulation, there is corresponding recoil of the column of blood against the valve, causing a loud and sharp pulmonary sound. This patient's urine has been examined, and has been found free from albumin. The test with nitrate of silver shows the usual absence of chlorides.

"The next case that I have to show you is one in which the conditions are materially different from those which we have just considered. This patient is a man, thirty-five years of age, of fairly good previous health, a car driver by occupation. His initial chill occurred three days ago; it was very severe, lasting, as he stated, more than an hour; it was followed by very marked prostration. From the moment of its occurrence there was a feeling of intense weakness; he took to his bed immediately, and, when removed to the hospital, had to be carried from his bed to the carriage, and from the carriage he was taken on a stretcher to the ward, and had to be lifted into bed. You find him now exhibiting the evidence of extreme muscular and nervous prostration. We place a glass of water in his hands, and in attempting to carry it to his lips he seizes the glass with both hands, nevertheless there is so much tremor that a portion of the water is spilled. The tongue is also tremulous. He is at

times delirious, with busy active delirum, a constant desire to get out of bed; but should he accomplish this, he would fall helplessly to the floor. His temperature on admission was 103.5° F., his pulse 132, and his respiration 30. The relative slowness of respiration, as compared with the pulse, shows that it is not the amount of lung implicated which constitutes the gravity of the affection; the pulse being so much more frequent than the respiration indicates that the cardiac ganglia and probably the heart muscle are directly affected by poison. On examining the heart we find that the first sound is extremely feeble, and the pulmonary sound is almost inaudible. The pulse is very small as well as frequent. It is stated that at the onset, immediately after the chill, there was vomiting. These conditions together indicate a very grave implication of the nervous system, showing an intensity of infection in marked contrast with that of the previous case. The urine also is found to be albuminous. On physical examination, we find on the right side dulness and tubular breathing in the summit of the lung, extending as far down as the fifth rib in front, and nearly to the angle of the scapula behind; in other parts of the lung there are a few moist râles, and also occasionally throughout the left lung. Still, the evidence of the physical signs is that the action of the respiratory apparatus is but moderately impaired. The gravity of the case depends upon the virulence of the infection, the direct poisoning of the nervous and muscular systems. The muscular weakness, which is so marked elsewhere, extends to the heart, as is indicated by the small and very frequent pulse, and by the character of the first sound. It is in this that the danger to our patient lies; it is not that his respiratory function is so far impaired as to create peril in that direction, but the danger is primary heart failure, due to the poisoning of the nervous system and of the muscular fibre. The whole heart in this case, both the left as well as the right side, is markedly feeble, and in our treatment the effort must be to keep up the cardiac action until the force of the infection is spent. Cases of this type are more apt to prove fatal during the stage of pyrexia. If we can tide them over until defervescence takes place the prognosis becomes much more favorable.

"Our next patient is a man sixty years of age, whose habits have been irregular, and whose constitution has been broken down by alcohol. He is now in the sixth day of the disease; the chill was not well pronounced; there was but moderate pain in the chest, but early in the case the difficulty of respiration became a prominent factor. We find him now with a temperature of 102° F., a pulse of 130, and with 48 respirations to the minute. The face is pale, the lips are blue, and the superficial veins are distended. On physical examina-

tion, we find that the lower lobe on the left side is for the most part consolidated; we find also that there are abundant mucous râles and perhaps a slight dulness throughout the remainder of the left lung, and also through the right lung. We have, therefore, a condition of pneumonic consolidation in the lower lobe of the left lung, with œdema more or less pronounced in the remainder of that lung and throughout the other. This condition necessarily implies a very grave impairment of the respiratory function. The amount of air which finds its way to the pulmonary vesicles is reduced to an extent which seriously threatens death by asphyxia. On examining the heart, we find by percussion that the right chambers are distended, the area of cardiac dulness being increased in the direction of the sternum. The pulmonary second sound is extremely feeble, being scarcely audible, obscured as it is by the mucous râles in that locality. The examination shows an increased area of hepatic and of splenic dulness, indicating that both the liver and spleen are distended with blood. The urine is albuminous. In short, we have everywhere the evidence of venous repletion. There is more blood in the veins and less in the arteries than in the normal condition. The obstruction to the pulmonary circulation calling upon the right ventricle for increased action, that portion of the heart is especially exposed to exhaustion.

"The leading factor in this case, therefore, is the impairment of the respiratory function with consecutive exhaustion of the right side of the heart. The danger is that the right heart will fail. And yet the original area of pneumonic consolidation was not great, not nearly so great as in the first case we examined. The difference lies in the condition of the circulatory apparatus, due, in the first instance, to the age of the patient and, in the second, to the alcoholic habit which has impaired the whole mechanism of circulation. With a vigorous heart and sound blood-vessels, the amount of pulmonary consolidation present would have constituted but a trifling danger. We have not in this case, either, the evidences of virulent infection, and the nervous system is not markedly implicated.

"When death occurs in such conditions the post-mortem shows the right cavities and the pulmonary artery distended with blood. In a private note which I received a few days ago from Dr. Daland, of Philadelphia, he describes the post-mortem appearances in four cases of this kind which he had observed. The right auricle and ventricle and the pulmonary artery were crowded full with a substance resembling currant jelly. The tendency to an early unfavorable termination in these cases is not so great as in the preceding type. Defervescence is not so marked nor so complete, and its occurrence does not affect

the prognosis so favorably. The mechanical conditions are but little affected by the temperature, and death often occurs when the pyrexia is very slight."

In addition to the foregoing types there may be differences in the clinical features of the disease depending upon mixed infections. Other organisms may be present with the pneumococcus lanceolatus, such as the pneumococcus of Friedländer, Pfeiffer's influenza bacillus, the Klebs-Loeffler bacillus, the typhoid bacillus, the staphylococcus pyogenes, and the streptococcus. One or more of these acting with the diplococcus proper to pneumonia may modify more or less the clinical picture.

The one most likely to take part is the streptococcus. It may be present from the beginning of the attack, or it may become associated at a later stage. If present from the first, the onset is likely to be less violent than usual, and the invasion more tardy in its movement. The sputum is more purulent, less vitreous, less sticky, and contains both organisms. The face is less flushed and has the aspect of sepsis. The temperature is irregular, and there is no crisis. Lysis may be extended over three or four weeks.

The upper lobe is more liable to be attacked, but the points of invasion change frequently, and the physical signs persist, perhaps for five or six weeks or longer. The cough is troublesome and there is great prostration. It is often months before the health is regained. And yet, with all this, the percentage of mortality is rather less than in pure pneumococcic infection.

Weismayr reports 39 cases of pneumonia in which the pneumococcus lanceolatus was found alone in 34, and associated with the streptococcus in 2, while in 3 the streptoccocus was found alone. Of the 34 cases of pure pneumococcus infection 27 defervesced by crisis, 4 by lysis, and 3 proved fatal on the seventh, tenth, and twelfth days respectively, defervescence never being later than the eleventh day, excepting in 1 case when it was completed on the fifteenth day.

In contrast with this is the behavior of the five streptococcus cases. Of these one was fatal on the nineteenth day, and in the remaining four there was kept up an irregular remittent fever, lasting in one case until the thirty-seventh day. The signs of consolidation continued from nineteen to forty days.

The diagnosis of streptococcic pneumonia is based upon the atypical progress and long duration of the disease, but can be reached with certainty only by microscopical examination of the sputum.[22]

Pathology.

Autopsical Findings.

These correspond to a process extending from simple hyperæmia of the affected part through extreme engorgement, fibrinous and cellular exudation into the air cells,[1] complete consolidation, fatty degeneration of the exudate, and removal of the latter by absorption and expectoration. All of these stages may be represented at the same time in different portions of the lung. As to how far these changes correspond with the clinical phenomena of the disease, and the results of auscultation and percussion, it will be interesting to quote from a work which is at present a leading authority on the subject of pneumonia:[2]

"We may pause here to consider whether in a disease clinically so well defined as pneumonia, it be not possible to assign correctly the special anatomical changes which accompany the various periods or stages of the disease, such as are denoted by the pyrexia and physical signs. It is undoubtedly true that this can be done to a certain extent, but a little consideration will show a lack of absolute parallelism between the anatomical and clinical features. At the outset, the latter denote the existence of a more or less widespread area of congestion in the lung, as well as of incipient pleural inflammation, which are conditions of structural change possible to be detected in the dead body. Yet there must be a condition antecedent to these changes that constitutes the so-called 'first stage,' for which there is no anatomical indication. Indeed, as we have seen, the stage of pulmonary engorgement has seldom been clearly demonstrated anatomically; for the obvious reason that at this early period of the affection death rarely occurs, and also because in cases which run the most rapidly fatal course their very intensity carries them beyond this stage before death. And as has been pointed out, it is extremely difficult to infer from post-mortem appearances the existence of ante-mortem congestion in any organ, and especially in an organ like the lung, which is so readily influenced by the circulatory changes that arise in the last hours of life, or in the act of dying. It is well known how at this time the blood tends to accumulate in the venous system, and to be especially prone to collect in the dependent parts from the failure of the heart to propel it onwards; and this resulting condition of hypostasis is even more liable to occur when the heart is already weakened by the febrile process. The lung may become so filled with serosanguinolent exudation as to be quite solidified, and the term 'hypostatic pneumonia' has been employed to denote this."

The earliest lesion is simple hyperæmia. When the chest is opened in a case in which death has occurred from pneumonia a portion of the lung may be found in this condition. It is seen not to be so fully collapsed as the surrounding normal lung, and to the touch it is slightly more resistant. The color is bright red, modified by the natural pigmentation of the lung. The pleural surface has lost some of its brilliancy, the epithelium being cloudy or perhaps exfoliated. On section, the surfaces are bright red, and exude a bloody frothy serum. The physical sign corresponding to this condition is scarcely more than a slight localized feebleness of respiration, with more or less abundant moist râles. A few hours later, the hyperæmia has passed into an extreme degree of vascular engorgement. The diseased part shrinks but little when the chest is opened. The pleural surface is of a deep red color, veiled by more or less of fibrinous exudate, which peels off readily in flakes. A similar condition is often observed on the corresponding costal surface. The resistance to the touch is markedly increased, and on section the tissue is more readily divided than in healthy lung. The cut surfaces are dark red in color, and dark blood mingled with air follows the knife. The appearance resembles closely that of an incised spleen, and the term splenization is applied to this stage of the local disease. At points minute extravasations of blood may be observed in the substance of the engorged tissue. Microscopically, the pulmonary capillaries will be found distended with blood, more or less fluid occupying the air cells.

But the lung still crepitates between the thumb and finger, and can be squeezed dry without breaking down. A piece of it thrown into water floats.

The physical signs belonging to this condition of the lung are diminished resonance on percussion, bronchovesicular respiration, crepitant râles, and slightly increased vocal resonance. In addition a pleural friction sound is often present.

The distinguishing feature of the next stage is the filling up of the air cells with a fibrinous exudate by which the parenchyma is completely solidified. If a considerable area is involved the lung is increased in bulk and pushes out into the intercostal spaces, so that furrows are imprinted on its surface by the ribs. The lung is usually covered by a dense white, or grayish, or yellowish layer of fibrin, which if removed shows a deep mottled red or purple color beneath. This layer is adherent to the costal pleura also, and the separation leaves both the pulmonary and the costal surfaces rough and irregular. Osler[23] states that the pleural exudate may form a creamy layer an inch in thickness. When cut into, the solidified mass is found to

have much the consistence of liver, and to be dark red or brownish-red in color; and for this reason the condition is known as *red hepatization.* In asthenic cases the proportion of fibrin in the exudate seems to be less, and the hepatized portion is flabby as compared with what is seen in cases belonging to the sthenic type. The cut surface has a granular appearance due to the projection of the little

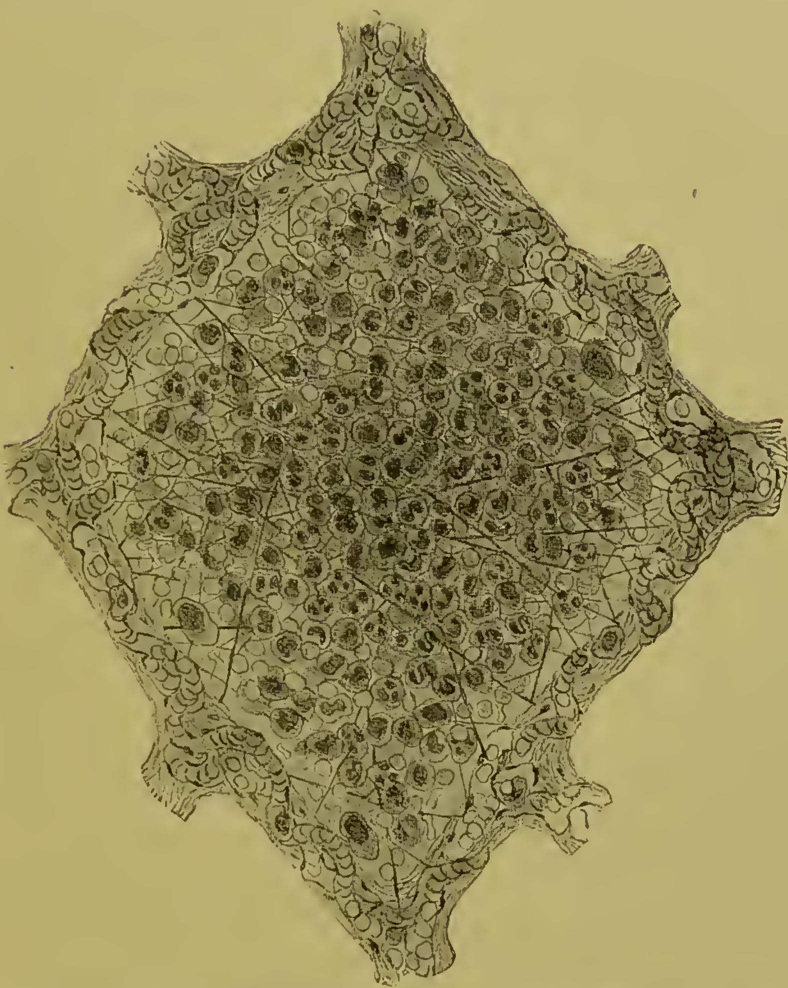

FIG. 2.—Air-cell Filled with Pneumonic Exudate. (Drawn by Dr. Louise Cordes from a specimen in the laboratory of the Presbyterian Hospital, New York.)

plugs of fibrin with which the alveoli and the bronchioles are filled. These can readily be scraped from the surface of the section, and are found to be casts of the air cells intermixed with cylindrical moulds of the ultimate divisions of the air tubes. The infiltrated tissue does not crepitate on pressure, is friable, and can be torn much more readily than normal lung structure. Where a bronchial tube is cut across a sticky mucus of variable color flows out. A piece of hepatized lung sinks in water.

During this stage the weight of the lung may reach 2,500 or 3,000 gm., instead of 600 gm. which is the normal average.

Microscopically the moulds of the alveoli already alluded to are found to consist chiefly of fibrin in the form of a delicate mesh, to which are added red blood corpuscles, leucocytes, epithelial cells, and numerous diplococci pneumoniæ. Other organisms, such as streptococci, staphylococci, etc., are often found associated with the specific microbe.

As this stage approaches completion the capillaries derived from the pulmonary artery become occluded, and the resulting thrombosis extends backwards into the larger vessels, even as far as to the giving off of the branch supplying the lobe. Indeed, there are cases on record in which the thrombus has reached the bifurcation of the pulmonary artery itself, and a portion of the clot has broken off and been swept into the sound lung, causing immediate death.

This stoppage of the functional capillary circulation is perhaps due in part to vital changes growing out of the microbic invasion, but the chief agency is the pressure exerted by the exudate. The tension in the pulmonary circulation being scarcely half that in the systemic, a comparatively slight mechanical cause is sufficient to arrest the movement of the blood.

The septa between the air cells are but little changed beyond the above-mentioned engorgement of the vessels and perhaps some loss of epithelium. In their migration from the capillaries some of the leucocytes remain entangled in the stroma. The nutritive vessels remain pervious.

The pleura at this stage is usually covered by a dense layer of false membrane, which dips also into the interlobar fissures, and bridges them over. This layer of fibrin very generally extends beyond the area of hepatization, becoming thinner towards the edges of the patch. It may cause an adhesion of the two pleural surfaces, which latter, however, are easily torn apart.

The physical signs indicating the existence of hepatization are dulness, approaching to flatness, and increased resistance on percussion, with tubular breathing, or perhaps entire absence of respiratory sound if the exudate extends far into the tubes. To this is added increase of vocal resonance and of vocal fremitus.

Succeeding the stage of red is that of *gray hepatization.* The change results from the absorption and removal of much of the coloring-matter of the red cells in the exudate, the addition of white corpuscles in great number, and a disintegration of the formed elements comprised in the contents of the air cells into a fatty, granular material. As the term indicates, the color of the cut surface is changed

from red to gray, but as the change takes place irregularly the color is more or less mottled. In consistence the tissue is softer than in the previous stages, so that the finger may be thrust into it, and the pit thus formed fills with a dirty puriform fluid. This becomes more marked as the change progresses, and the cell contents become more liquid. The term purulent infiltration is applied to this condition incorrectly, as the fluid is not pus but a fatty and granular detritus.

Some confusion, however, has arisen in regard to the condition to which the term *purulent infiltration* properly belongs. By some this is considered as merely an advanced stage of gray hepatization, the fibrin and the red cells in the exudate having broken down and the leucocytes undergoing fatty degeneration. These authorities regard the condition as a step in the progress toward resolution, a preparation of the exudate for being absorbed.

Other authorities describe purulent infiltration as one of the issues of pneumonia, and almost necessarily fatal. To them it means a diffuse suppuration of the affected portion of the lung, an event so grave as practically to preclude recovery.

It is not difficult to see how this confusion has arisen. Necessarily our knowledge of the local conditions has been obtained from the post-mortem findings, and these may admit of either interpretation. But it seems to me that there are two distinct processes, the results of which may be differentiated both by the clinical history and by the changes found in the lung.

We may find a subject whose expectoration had gone through the usual changes and become mucopurulent, and who had passed the crisis, but has not been able to rally afterwards. Death has taken place from mere exhaustion. The autopsy shows the cell walls intact, and the cells filled with the grayish material, which gives the name to this stage of hepatization.

In another case the creamy sputa will have made their appearance in due sequence, and soon afterwards there will have been a more or less complete defervescence, but the temperature has not remained down. There have been fluctuations resembling those of hectic, with chilliness and perspirations. After a course of several days death has taken place under these septic manifestations. The autopsy shows the affected area filled with a creamy fluid identical with pus, and the septa infiltrated, softened, and more or less broken down.

Now in the first case death has overtaken the patient in the midst of a process tending to restoration to a normal condition. In the second, the restorative action had been interrupted by a new process with its seat in the cell wall. The nutritive vessels have been at-

tacked, and there has supervened a veritable "inflammation of the lungs," going on to suppuration and breaking down of tissue. To this condition the term purulent infiltration is very applicable, and it will be readily apparent that such extensive suppurative action involving corresponding loss of lung substance and coming upon the heels of an exhausting pyrexia could scarcely be recovered from.

There is no physical sign by which the transition from red to gray hepatization is indicated. If resolution begins in this stage it may be marked by a return of the crepitant râle. But resolution may take place before this stage is reached, and in that case the return of crepitation would be during red hepatization.

As to the time at which these several stages develop the greatest diversity obtains, and in this connection the interest of the following note is such that no apology is necessary for its insertion:

"As illustrating the variability of the anatomical characters of the inflamed lung at the time of death, and the lack of any definite relation of these to the time at which death has occurred, the following cases may be quoted, in which death took place at periods varying from six to seventeen days from the onset.

"1. Male, aged 40, death on sixth day. Gray hepatization of greater part of left lower lobe.

"2. Male, aged 75, death on seventh day. Gray hepatization of anterior part of upper lobe (congested posteriorly) and of upper one-fourth of lower lobe of right lung. In left lower lobe a 'recent' pneumonic nodule.

"3. Male, middle-aged, death on seventh day. Whole of lower and part of upper lobe of left lung hepatized; gray at base, elsewhere red.

"4. Male, aged 4, death on seventh day. Gray hepatization and 'purulent infiltration' of right upper lobe.

"5. Male, aged 62, death on eighth day. 'Red passing into gray' hepatization of right lower lobe.

"6. Male, aged 50, death on eighth day. Gray hepatization of right lung (except apex).

"7. Male, aged 24, death on ninth day. Gray hepatization of left upper and lower lobes. Patches of 'reddish-gray' hepatization in right upper and lower lobes. (Fibrinous coagula in bronchi.)

"8. Female, middle-aged, death on ninth day. 'Grayish-pink' (early gray) consolidation of right upper and lower lobes.

"9. Male, aged 48, death on tenth day. Right lung, except extreme apex and anterior margin, entirely in state of gray hepatization.

"10. Female, aged 4, death on the tenth day. Lower and part of upper lobe of right lung in state of 'reddish-gray' hepatization.

"11. Male, aged 18, death on thirteenth day. Both lower lobes 'dark colored and granular.' (This case was rheumatic, and was accompanied by peri- and endocarditis.)

"12. Male, aged 50, death on sixteenth day. Gray hepatization, studded with yellowish points, of whole of right lung, except anterior and lower margins. [Probably consecutive "pneumonitis" A. H. S.]

"13. Male, aged 4, death on seventeenth day. Gray hepatization of left lower lobe." (Sturgis and Coupland.[2])

According to Delafield and Prudden,[24] the lung is found passing from red to gray hepatization at any time between the second and the eighteenth days of the disease. It is found completely gray at any time from the fourth to the twenty-fifth day. In about one-half of the fatal cases death takes place in the condition of red and gray hepatization; in about one-fourth in the condition of gray hepatization.

As resolution progresses the infiltrated material is gradually removed, and little by little the air regains access to the alveoli. The lung tissue becomes less friable, shrinks in volume, is more elastic, crepitates again on pressure, and resumes a more natural color. Corresponding with these changes the physical signs which marked the invasion reappear in reversed order. Percussion dulness becomes less absolute, and bronchial breathing, if previously all respiratory sounds were absent, returns for a time, and then gradually gives place to vesicular respiration accompanied at first by crepitation. Vocal resonance and vocal fremitus are less marked. It is a long time, however, before the physical signs get to be entirely normal, especially if the fibrinous layer covering and uniting the pleural surfaces is of considerable thickness, thus dampening the percussion note and obscuring the auscultatory sounds.

In most cases besides the specific pneumonic lesion, which is limited to a certain area, there will be found evidence of congestion in other parts of the same lung, and perhaps in its fellow. This congestion may be so intense, and the resulting secretion so abundant, as to leave insufficient breathing surface, and to be the immediate cause of death. The congestion may be hypostatic, when it will be limited to the dependent portion of the lung, or it may be due to cardiac weakness, and affect all parts. Very frequently more or less pulmonary œdema is present.

In rare instances the affected portion of the lung undergoes a suppurative process. The surface has then a yellowish color, and on section a purulent fluid exudes. The cells, resembling pus cells in all respects, not only fill the alveoli, but infiltrate the interalveolar walls.[25] The pressure thus induced interferes with the nutrition of the septa, and may lead to their softening and breaking down. This may result in the formation of abscesses, but the condition if at all extreme usually proves fatal before this point is attained.

Abscess of the lung as an event of pneumonia occurs in between one and two per cent. of all cases. The abscess may have firm walls, or may be only an irregular cavity in broken-down tissue. Abscesses vary in size from that of a pea to the dimensions of the entire lobe.

They sometimes discharge through a bronchus, at other times, when small, they become encapsulated and undergo caseation.

After death from pneumonia a characteristic condition of the heart is usually found, in which the left cavities are nearly or quite empty while the right cavities are distended by firm coagula that often extend into the branches of the pulmonary artery.

The spleen is often enlarged, especially in asthenic cases in which the infection has been intense. Under like conditions the liver is congested, particularly when the respiration has been greatly embarrassed and the right heart overtaxed.

In the kidneys the cells lining the tubes are often in the condition of cloudy swelling, and in a small proportion of cases there is fully developed nephritis.

There is a form of pneumonia[28] in which the air cells, instead of becoming entirely free as the result of resolution, are found to contain more or less of connective tissue springing from the cell wall and in intimate connection with it. This is not uniformly disseminated through the air vesicles, some of these containing only fibrin and various cells. The connective tissue may become organized, the new vessels communicating with the vessels of the septa.

The clinical history is somewhat different from that of ordinary pneumonia, being more protracted, and the phenomena of crisis are not well marked. The process realizes the idea of a true pneumonitis. If life continues for several months, the air spaces become completely filled and their walls much thickened; and smooth connective tissue takes the place of the natural structure of the lung.

Pathology.

It is now very generally conceded that the essential phenomena of pneumonia are due to the action of one or more forms of bacilli. In nearly every case the diplococcus pneumoniæ of Fränkel is found in the exudate, and it may also in rare cases be disseminated through the system more or less generally. With this are sometimes associated other microorganisms in such number as to suggest the probability that they play an important though subsidiary part both in the local process and the general infection.

As to the relation of the specific organism to the disease as a whole, we may note:

First, that no amount of traumatism inflicted upon the lung, be the methods ever so varied, produces pneumonia. We may cut, pierce, bruise, burn, or scald the lung; we may introduce mechanical or chemical irritants into the air passages, and while we get inflammation as the result we do not get pneumonia.

Second, we may have pneumococcic infection in several serous and synovial cavities at the same time, resulting in suppuration in each, and not have pneumonia.

Third, we may introduce the pneumococcus into any portion of the body save the lungs, and even into the blood itself, and we do not get pneumonia.

Fourth, but if we introduce active pneumococci into the parenchyma of the lung we always get pneumonia as the result.

Fifth, in probably every case of pneumonia coming to autopsy during the active stage, if the search is properly conducted, the presence of pneumococci in the lungs can be demonstrated.

The inference from these facts is that the one thing necessary for the development of pneumonia is the presence in the alveoli of pneumococci in a condition of active multiplication.

In regard to the nature of the local lesion, while it is commonly designated as an inflammation, the term is scarcely correct in the sense in which it is understood when applied to that process as it occurs in other structures. We consider inflammation as affecting the tissue itself, and causing an anatomical change in its elements. But in pneumonia the interalveolar septa seem to be but little affected by the enormously active process taking place within the cells. After a few days these cells are emptied of the mass of exudate with which they were filled, and the cell walls are found practically in their normal condition, having suffered at the most only a little loss of epithelium. Had this been an ordinary inflammation, as of the liver or the kidneys, accompanied by a corresponding amount of local change, we should expect to find such damage to the part as would require a long process of repair, if, indeed, complete recovery could ever take place. Vessels would be obliterated, new connective tissue would be formed, permanent indurations would remain, etc. Indeed, such changes are the usual accompaniments of chronic pulmonary inflammations, and sometimes remain after pneumonia of an aberrant type. That they do not occur in typical croupous pneumonia seems sufficient evidence that the process in the latter case is essentially different from inflammation in general.

But if other evidence were needed it is supplied in the fact that at the crisis the fever, which if the process were an inflammation we should have to regard as an inflammatory fever, ceases abruptly, while the so-called inflammation goes on. In typical cases there comes a time, usually from the fifth to the eighth day, when the temperature falls suddenly nearly or quite to the normal line, while the physical signs denote that the local conditions remain unchanged. In what inflammation occurring elsewhere, and of sufficient intensity

to occasion a temperature of 103° to 106°, do we find such a defervescence with all the local signs of the inflammation persisting afterwards?

But if this is not an inflammation of the lung tissue, what is it? This question has received various answers. It has been suggested that the fever is the primary affection and that the changes in the lung bear some such relation to it as the rash of scarlatina, for example, bears to the fever that accompanies it. The term lung fever is a survival of this view.

It has even been suggested by Trousseau that the process is essentially a form of erysipelas, modified by the peculiar structure in which it has its seat. And again it has been thought to be a herpes zoster of the lung, having a nervous origin. But even these fantastic suggestions, designed to meet the difficulties in the way of regarding pneumonia as a simple inflammation, still leave the phenomena of the crisis above referred to unexplained.

The discovery of the pneumococcus has carried us along so far as to enable us to say that pneumonia is an infectious disease depending upon the action of this organism. This is a great advance, but it still leaves the question open, How does the micrococcus bring about the local and general conditions? How does it find its way to the lung, and when it gets there, how does it act?

It seems to the writer that there is an answer to this that is at once consistent with the facts and affords a satisfactory explanation of the phenomena observed. It is that instead of an inflammation of the lung tissue we have essentially a process of germ culture going on in the air cells. To make this intelligible, we must recall the fact that in the lung we have two separate and distinct circulations, the one derived from the bronchial vessels, and designed for the nutrition of the structure; and the other derived from the pulmonary vessels, and devoted to the function of the organ. It being chiefly with the latter that the pathological process has to do, while the former is left to maintain the integrity of the tissues, we can see that a diseased and a relatively healthy action may go on side by side, dependent upon the condition of the respective systems of vessels.

Let now a diplococcus find its way into an air cell, and there excite an irritation in the delicate structure that separates the interior of the cell from the functional blood supply. An exudation from the latter follows, and the coccus at once finds itself surrounded by a medium suitable for its multiplication. The conditions as to temperature, etc., are similar to those in artificial cultures in the laboratory. The microbes increase rapidly, more exudate is poured into the cell, which becomes filled and overflows into an adjoining

cell, where the process is repeated, cell after cell and lobule after lobule being invaded. All this time the cell wall is nourished by its nutrient blood supply, and is almost as indifferent to what is going on in the space which it encloses as is the glass of the culture tube to the process within it.

If asked what, after all, is the evidence that the process does not affect both circulations alike, the answer is, that if it did so, the resulting condition would be incompatible with the maintenance of vitality in the affected part. We have, for example, a portion of hepatized lung, perhaps as large as a child's head, in which the branches of the pulmonary artery are thrombosed, and into which no blood from the right side of the heart can penetrate. Suppose for an instant that a like condition existed in the nutrient circulation, that its vessels also were occluded, and that no blood could reach the parenchyma of the lung from the left side of the heart. So large a mass could not be nourished by imbibition from surrounding parts, and there would be nothing left for it but speedy loss of vitality. What actually does happen, however, is, as we have seen, that the cell wall escapes without injury, and not only so, but the absorptive apparatus remains in full activity as is proved by the quickness and completeness with which the removal of such a bulk of material is effected.

From the moment that the culture process begins, the specific toxin also begins to be formed, and is at once absorbed into the circulation. From this we have the chill, the high temperature, the prostration, and all the other evidences of a virulent infection. The rapidity with which the toxic product finds its way into the system is explained by the favorable conditions presented by the great vascularity of the lung and the enormous surface from which absorption takes place. Indeed, it would almost seem as if the lung structure were arranged with a view to such a result.

So long as fresh supplies of toxin are being formed, or, in other words, so long as the consolidation is spreading, so long the toxæmia will be maintained. But here again, as in artificial cultures, there is a limit beyond which the process cannot extend. A given quantity of a culture medium can maintain the life of a given number of germs only for a certain time. Beyond that time the changes produced in the medium render it unfit as a soil for the further growth of the organisms, and the death of the latter puts an end to the process. With the supply of toxin cut off the temperature falls. If the invasion has been regular and rapid, coming to an abrupt termination with the complete consolidation of the lobe, the supply of the toxin will cease abruptly, and we shall have defervescence by crisis. If,

on the other hand, the effusion into the air cells has been gradual, and the process of consolidation slowly carried forward, the supply of toxin will continue in one part while it fails in another; the process will be prolonged, and the defervescence will be by lysis.

This does not exclude the theory of the production of an antitoxin. Indeed numerous observations, and especially those of the Klemperer Brothers (see page 124) go to show that a transient immunity is created by an attack of pneumonia, and that this immunity may be transferred to another subject by serum inoculation. This could scarcely be explained except on the theory of an antitoxin, and I can see no obstacle to accepting both theories in explanation of the clinical phenomenon in question.

As bearing upon the formation of an antitoxin the following observation by Pinna[26] is of interest: He found that the pus obtained by injecting turpentine into the cellular tissue of a man, and which pus was absolutely sterile, had the power when injected into rabbits of rendering the animals immune to inoculations of pus containing pneumococci. The rabbits recovered and remained healthy, while others not so protected succumbed to pneumococcus septicæmia within thirty-six hours after receiving a like amount of pneumonic pus. It would seem from this that the pus itself, apart from any microbic action, possesses antitoxic properties.

This suggests the probability that the exudate during the process of retrogression assumes the character of simple sterile pus in its relation to the pneumotoxin. The theory of an antitoxin will be further discussed in treating of serum therapy.

But the matter is still further complicated by a chemical factor that enters into the case the moment the current in the functional capillaries is arrested. Normally there is carried in these vessels a varying amount of sodium bicarbonate held in solution in the blood. It is requisite that the carbon dioxide contained in the bicarbonate should be set free in the lungs, in order that it may escape with the expired air. Nature provides for this by the production of a special organic acid in the parenchyma of the lung, known as pneumic acid. This combines with the sodium, and the carbon dioxide thus liberated passes into the alveoli.

But when the functional circulation ceases, the sodium bicarbonate is no longer at hand to neutralize the pneumic acid, which continues to be produced as a part of the nutritive process. The parenchyma of the lung, therefore, becomes saturated with a free acid, and the slightest trace of acid in the medium is, as has been proved from laboratory experiments, fatal to the propagation of the pneumococcus.*

* The acid reaction of hepatized lung has been demonstrated in the cadaver.

Thus there are three things that tend to bring about the crisis: failure of the supply of toxin, the formation of an antitoxin, and the presence of a free acid in the affected part inhibiting the action of the diplococcus.

Probably the phagocytosis of Metchnikoff also plays a part, the phagocytes destroying the pneumococci. This, however, is only conjectural.

With regard to the mode of access of the germ to the air cell there are only three channels by which it might reach the seat of its activity in the lung. These are the blood-vessels, the lymphatics, and the air passages. As to the first of these it has been amply demonstrated that the pneumococcus may find its way into the blood-vessels, and may set up a peculiar action in localities that are shut out from all communication with the exterior of the body. Thus it is sometimes found in the fluid of pericarditis, and in the pus of meningitis, the lung not being at all implicated. We must therefore concede the possibility of its reaching the lung in this way; but is this the usual route? Against this supposition is the fact that in the vast majority of cases of pneumonia the local infection is strictly limited to the lungs, although, as we have seen above, the organism is capable of attacking other structures. Moreover, if we were to admit a selective action on the part of the lungs whereby the coccus is attracted, as it were, to the pulmonary structure (as the gonococcus is, for example, to certain tissues), we still have to account for the fact that as a rule the morbid process begins in a single focus in the lung and spreads from that as a centre, instead of attacking different places in the lungs, as it would be likely to do if the organisms were floating in the blood. When we add to this what the researches of Kanthack [27] and others prove, that if in a case of pneumonia the pneumococci are found in the blood, and can be cultivated from it, the prognosis is bad, while, as we know, under usual conditions a large proportion of cases of pneumonia terminate favorably, we have a strong probability, to say the least, that the blood-vessels are not the usual channel by which the infection reaches the lung.

As to the lymphatics, the same reasoning holds good, and in addition we have the extreme improbability that the organisms could pass the barrier of the lymphatic glands.

This brings us back to the air passages as the most likely avenue of infection.* But this is by no means an open one. The anatomical

* As corroborative of this view of the mode of access of the infecting germ it is interesting to observe that as in two-thirds of the cases foreign bodies passing down the trachea find their way into the *right* bronchus, owing to its greater width, so we find in practice a very considerable preponderance of right-side pneumonia,

configuration of the bronchial tree is such that it is impossible that a solid particle, however minute, should be carried with the inspired air beyond the second or third divisions without coming into contact with the bronchial wall. Even gaseous material cannot pass from the glottis to the alveoli at a single inhalation. It is only by a series of inspiratory impulses, aided at last by molecular interchange between the inspired and the residual air, that it can reach the air cells.

Once deposited upon the mucous surface of the tubes all the conditions favor the expulsion of a solid particle rather than its further progress inward. In respiration the outward current is much more rapid than the inward, and expiration tends therefore to drive backward with a greater force than inspiration exerts in drawing forward. To this constant outward impulse is added the action of the ciliated epithelium, by which a movement in the direction toward the glottis is imparted to the fluid which bathes the bronchial mucous membrane. These influences combined render it extremely difficult for any solid substance, however minutely divided, to be carried into the alveoli by simple inhalation.

This provision of nature for preventing access of foreign material to the air cells is so complete that they are very seldom invaded by even the finest particles that are carried in the atmosphere.

Doubtless this provision is operative to a very great extent in protecting the lungs from the ingress of pathogenic germs. These may appear in the mouth and pharynx, where the epithelium is of the pavement variety, but when they reach the point where the ciliated epithelium begins, the action of the cilia opposes their further progress. But for this we should find all manner of germs disseminated over the whole extent of the respiratory tract, instead of being confined, as a rule, to the regions above the glottis and to the larger bronchial tubes.

But this protection is not absolute at the best, and is liable to be impaired by any cause that affects the bronchial mucous membrane. Thus, for example, the efficiency of the ciliary movement is lessened during the early dry stage of a common cold, and in bronchial catarrh.

Even if the protection remained intact it would not prevent the spread of microorganisms over the bronchial mucous surface by the process of multiplication, which process acts with inconceivable rapidity under favorable conditions. A single microbe lodged in one of the smaller tubes, and there finding a suitable culture medium in the secreted mucus, would in a few hours produce millions of its

probably the result of the same anatomical condition by which germs on reaching the bifurcation in their passage downwards are influenced to pass into the right bronchus rather than the left.

kind. The colony spreading in this manner would not be long in reaching the vesicles. Here the epithelium is of a different character, resembling closely the type of serous membranes, which are prone, under irritation, to yield a fibrinous exudate. In the alveolus, however, this form of exudate appears from present indications to be the product of only one form of irritation, viz., that resulting from the presence of microorganisms. It seems to be afforded principally, if not wholly, by the *pulmonary*, as distinguished from the *bronchial*, capillaries. When there is infiltration into the septum from its *nutrient* vessels the infiltration is corpuscular and not fibrinous.

As has already been seen, the pneumococcus lanceolatus is present in the mouth and nasopharynx in perhaps the majority of healthy persons. Dr. Neumann's studies made at my instance show that in three out of sixteen autopsies in persons dying of other disease than pneumonia this organism was found in the smaller bronchi, say, of the fourth or fifth division. Why in such subjects they do not always penetrate into the air vesicles and excite pneumonia is a question of great interest, the answer to which is not at hand. That they do so penetrate under certain conditions we already know, but what the conditions are, and how they act, we cannot tell. In general terms, their presence in the air cells seems to be associated with depression of vitality, as if the protection against their entrance was sufficient so long as the vigor of the subject remained unimpaired, but failed when it was diminished. Starr[28] suggests that the pneumococcus becomes more virulent after exposure to cold.

It will be urged against this view of what takes place in the pneumonic lung that there is no necessary relation between the amount of lung involved and the degree of toxæmia. This is true as a simple proposition; but in this as in all other forms of toxic infection, different persons show remarkable differences in susceptibility to the poison, and at the same time the poison itself varies extremely in virulence.

Furthermore, accepting the theory of an antitoxin, the period at which the formation of this substance begins in a given case and the rate at which it progresses, become at once factors in determining the general condition of the patient at a given time.

But perhaps the most important consideration in this connection is that the area in which the toxin is being formed may greatly exceed that in which physical signs can be detected. The thinnest film of exudate will be a sufficient medium for the growth of microbes, and that under conditions most favorable for a rapid absorption of the poison they afford. So that while there may not be material enough in the bronchioles and alveoli to change the percussion note,

or to give rise to crepitus, it may still be the source of very active infection.

Keeping these points in view we may safely say that, other things being equal, the systemic impression will be closely proportioned to the extent of the local invasion.

Occasionally in the progress of a pneumonia, gangrene of a portion of the lung takes place. We may assume that in these cases a branch of the bronchial artery becomes involved in the process, thus shutting off the nutrient circulation from the corresponding portion of lung tissue. That this does not occur more frequently shows how passive is the rôle played by the pulmonary parenchyma.

A process of less intensity involving the nutrient vessels would account for the permanent change found in chronic pneumonia.

Suppuration with the formation of abscesses in the lung tissue is now and again observed. This is probably due to a mixed infection, in which pyogenic germs take part with the diplococcus and produce a more intense degree of local irritation involving the lung structure itself.

The evolution of new germs having ceased, and the system having recovered in a measure from the depression of the toxæmia, the process of the removal of the exudate from the air cells begins. This is accomplished chiefly by absorption, and is facilitated by the liquefaction of the fibrin and the granular disintegration of the corpuscular elements which characterize the stage of resolution.

In the course of a few days, if all goes well, the cell is entirely relieved of its contents. Its walls remain intact and ready for an immediate resumption of function.

The sum of the argument, finally, is that from its peculiar construction the lung is enabled to afford a field for bacterial culture and to supply a culture medium, and this without calling upon its own nutritive resources, or directly compromising its own tissues. It is the fact that in the lung there are empty spaces accessible to bacteria, and separated from an unlimited blood supply by only the thinnest and most permeable wall, that makes the phenomena of pneumonia possible. It is the further fact that the framework between these spaces has its own separate blood supply, apart from the vessels involved in the pneumonic process, that prevents a sweeping destruction of the lung tissue.

In no other organ in the body is such a mingling of structural health and diseased action conceivable, for in no other organ is the blood supply for nutrition and function separately provided for.*

* A somewhat analogous condition is met with in the heart, inasmuch as blood flows through its cavities for functional purposes, while its nutrition is supplied

The sequence of events taking place in an attack of pneumonia would seem to be as follows:

1. The occurrence of some cause of depression, either local or general, which favors the germination of pneumococci, already present in some one of the smaller tubes.

2. The formation of a colony that spreads until it reaches the group of air vesicles that are terminal to the tube in question.

3. The setting up of an irritation in these vesicles, causing a fibrinous exudation, an emigration of leucocytes, and a diapedesis of red cells from the functional capillaries.

4. The formation of a colony of pneumococci in the medium afforded by this exudate.

5. Arrest of the blood stream in the functional capillaries, followed by accumulation of free pneumic acid in the parenchyma of the affected area.

6. Overflow of exudate into neighboring lobules, starting the process in them also.

7. Arrest of germ growth by exhaustion of the medium and the accumulation of free acid in the tissue of the lung. Up to this time there has been a constant formation and absorption of toxin.

8. Retrogressive changes in the exudate preparatory to its removal by absorption.

9. Probably, in this latter process, formation of an antitoxic principle.

10. Entire removal of the exudate and restoration of the vesicle to its normal condition.

11. Resumption of the functional capillary circulation.

The physical signs of pneumonia being in a typical case so distinctive, we are liable to fall into the error of considering that the disease is not present until some one or more of these signs can be made out. But, regarding as the first step in the process the invasion of the air cells by the germ, pneumonia is present the moment the first lodgment is effected. Investigation has shown that the pneumococcus is most active in creating toxin at the earliest period of its life, and also that the toxin it produces is then most virulent. Hence, we can understand that an amount of exudate not yet sufficient to be detected by the physical signs would still be sufficient to afford a medium for the growth of cocci in adequate numbers to poison the system with their toxin. Until such poisoning reaches a point at which general symptoms are manifested, fever, chill, etc., there may

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through the coronary vessels. It would be a legitimate, if gross caricature of the old idea of pneumonitis if one should find a heart with its cavities filled with fibrinous clots and should label the specimen *carditis*.

be nothing to indicate what is going on in the lung except perhaps prodromes, which may or may not arrest the attention of the patient. In other words, an important stage of progress may be reached before the disease is openly declared. This explains those cases of very sudden invasion, as, for example, one cited by Sturgis, in which a person started to cross London bridge from the Surrey side without pneumonia, but had pneumonia when he reached the City.

The conditions for rapid absorption of the poison are best when the air cell is but partly filled; later, when the cell is crowded with exudate, and the affected portion of lung is distended beyond its natural bulk, the pressure renders absorption less active. At the same time, as the germs grow older, the toxin becomes less virulent, and a time arrives when the fully hepatized portion ceases to be an unfavorable factor in the case except for the breathing surface it withdraws from use. On the contrary, it may be that the older germs now reverse their rôle and begin the production of an antitoxin. Were it not for the fresh growth constantly spreading about the circumference of the hepatized portion and extending in a wider circle than that indicated by the physical signs, the infection would soon come to a standstill and crisis would result. As it is, the crisis is deferred until the infecting are balanced by the disinfecting forces, the latter including the various emunctories by which the poison is discharged from the body.

Bacteriology.

The history of the pneumococcus is interesting in that the organism was known for some time before its connection with pneumonia was suspected. During this interval it received various designations, such as micrococcus Pasteuri, micrococcus of sputum septicæmia, bacillus septicus sputigenus, etc. Later, when its pathogenic relations had been established, it received more specific names—diplococcus pneumoniæ, pneumococcus capsulatus, pneumococcus lanceolatus, pneumococcus of Fraenkel, micrococcus pneumoniæ crouposæ.

In 1880 Sternberg discovered to his surprise that his saliva, he being in perfect health at the time, was fatal to rabbits if injected into the cellular tissue, death taking place within forty-eight hours. Cultures made from the bodies of these animals resulted in the production of bacilli of a kind not before recognized, and inoculation with which was uniformly fatal. Waiving his right to give his own name to the new organism, he called it the micrococcus Pasteuri. These

observations were followed by others made by different bacteriologists and with results confirming the discovery of Sternberg. Netter found by inoculation experiments in rabbits that the saliva of one hundred and sixty-five healthy individuals showed the presence of this micrococcus in fifteen per cent. of the number.

In 1883 Talamon demonstrated the presence of this organism in the sputum of pneumonia, and produced pneumonia in rabbits by injecting material containing the germs directly into the lungs through the chest wall.

In 1886 Weichselbaum published the results of investigations showing the presence of the diplococcus in the fibrinous exudate of croupous pneumonia in the proportion of ninety-four cases in one hundred and twenty-nine. Since then it has been generally accepted that croupous pneumonia is an infectious disease caused by the pneumococcus lanceolatus, though other organisms may be associated with the latter.

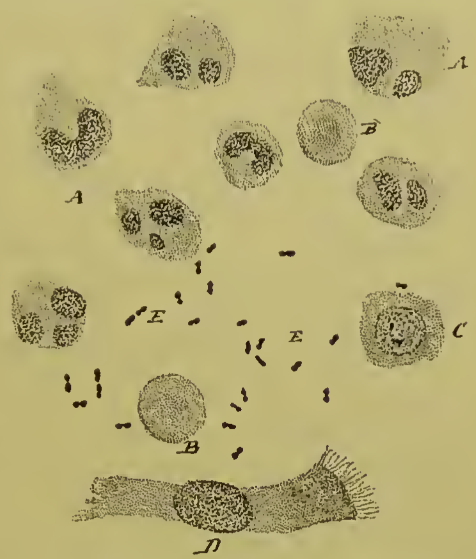

FIG. 3.—The Micrococcus Lanceolatus in Pneumonia Sputum. *AA*, Leucocytes; *BB*, red blood cells; *C*, epithelial cell; *D*, ciliated epithelium; *EE*, pneumococci. × 1000.

For the following description and the accompanying drawing I am indebted to Dr. George A. Tuttle, assistant pathologist of the Presbyterian Hospital, New York.

"The micrococcus lanceolatus, called also Fraenkel's diplococcus or pneumococcus, and diplococcus lanceolatus pneumoniæ, was first described by Sternberg in 1880 as the micrococcus Pasteuri. He noted its very frequent presence in normal saliva and demonstrated its virulence by animal inoculations. A. Fraenkel confirmed the observations of Sternberg, and noted the presence of this diplococcus in the rust-colored sputa of pneumonia, while it was absent in other acute inflammations of the lungs. He also obtained this organism, called by him the diplococcus of sputum septicæmia, in many cases of empyema following pneumonia and in the exudation of meningitis complicating pneumonia. In 1885–86 he was able to prove conclusively the causal relationship of this micrococcus to acute lobar pneumonia.

"The micrococcus lanceolatus in the blood of inoculated animals and in pneumonic sputum is generally seen in pairs of oval or lancet-shaped elements surrounded by a capsule of a substance resembling

mucin. In cultures short chains of three to four members are common, and at times longer chains of ten to twelve are seen, while the capsule is absent. There is a marked variation in the size and shape of the individual elements in cultivated specimens, and this peculiar characteristic is of considerable importance in distinguishing this organism from the streptococcus pyogenes which it so closely resembles in other respects. Like the other micrococci it is non-motile.

"It grows in all of the common faintly alkaline culture media, with or without the presence of free oxygen, at a temperaure of 35°–38° C. It will not grow at the ordinary room temperature, or on potato. On the surface of agar or of blood serum it forms minute, grayish, translucent colonies, at first resembling minute drops of water. In gelatin it grows rather slowly along the entire puncture and at the surface, the growth beneath the surface consisting of minute white colonies. It does not liquefy gelatin. It grows rapidly in milk, producing coagulation; also in bouillon, causing a slight cloudiness of the fluid and a little whitish sediment at the bottom of the tube. It loses its vitality in cultures on solid media in five to ten days; in bouillon its life is somewhat longer. By transplanting every fourth or fifth day the growth may be continued indefinitely in favorable conditions. The virulence of artificial cultures is rapidly lost, but can be restored by passing them through susceptible animals.

"It is readily stained with all of the aniline colors and by Gram's method. The capsule can be demonstrated in blood or sputum preparations by staining with carbol-fuchsin solution, and lightly washing with alcohol. The deeply stained diplococci will be seen surrounded by an oval colorless area representing the capsule."

This organism is found in the expectorated material in all but a very small percentage of the cases examined for it.* When appar-

* R. M. Pearce, in the Journal of the Boston Society of the Medical Sciences, for June, 1897, records that in 121 cases of acute lobar pneumonia the pneumococcus was found in the solidified lung in 110 cases, in 84 of which it was the only micro-organism present. In the remaining cases it was associated with varying frequency with the staphylococcus pyogenes aureus and albus, streptococcus pyogenes, Klebs-Loeffler bacillus, and the bacillus capsulatus (Wright). In some cases the association was with two of the above. Of the remaining 11 cases, in 8 the lung culture was not taken in 4, lost in 2, and sterile in 2, but in each of these there was general infection with the pneumococcus, and in 3 it was present in either pericardial or pleural exudate. This would justify the conclusion that the process in the lung was due to the same organism and was the source of the general infection. If, therefore, these cases are added to the others they make a total of 118 out of 121, or 97.5 per cent. due to the pneumococcus. In the exudate of acute pleuritis and acute pericarditis with pneumonia, the pneumococcus was found in every case in which examinations were made, 49 times in pleural exudates and 15 times in pericardial exudates. In various infections due to the pneumococcus, numbering

ently absent it is probable that faulty methods of search have been employed, or that some special circumstance has masked its development. When a pure culture is injected into the substance of the lung it invariably results in a typical croupous pneumonia. Injected into the cellular tissue or into the peritoneum it causes septicæmia.

The coccus growing rapidly is commonly inert at the end of a week. Probably this contributes, at least, to determine the crisis. It may also explain the benign course of pneumococcic infection in other tissues. Such infection of the pleura, for example, results commonly in a mild and tractable empyema as contrasted with infection from other pathogenic organisms of slower growths and more enduring vitality.

The pneumococcus exhibits great differences in virulence, suggesting that there may be several varieties. Inoculation experiments appear to show that one of these, the œdematogenic, causes local œdema with toxæmia. This is the variety most commonly found in pneumonia. Another produces abscess at the point of inoculation, and "is an exquisitely pyogenic microorganism." [29]

Eyre and Washbourn[30] in a very elaborate paper demonstrate that "there are a large number of types of the pneumococcus which differ from one another in virulence and in biological characters." The parasitic type, the typical pneumococcus, is the most virulent and also the least hardy and has the shortest life. The saprophytic type, such as is found in the mouths of normal individuals, is almost destitute of virulence, but is very hardy and long lived. By repeated passages through animals the several types may be made identical as to virulence, but in the case of the saprophytic type this virulence is reached and maintained with difficulty. The maximum of virulence, obtained by eight passages of the parasitic type and fifty-three passages of the saprophytic type, was such that .0000005 mgm. injected into the peritoneal cavity of a rabbit was fatal within twenty-four hours.

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55 cases, there were 26 acute infectious processes which were neither preceded nor accompanied by a lobar pneumonia. The cases comprised acute ulcerative endocarditis, acute purulent meningitis, acute fibrinous pericarditis, acute fibrinous peritonitis, and acute general infection with pneumococcus.

James J. Curry, of Boston, in the Journal of the Boston Society of the Medical Sciences, for March, 1898, mentions two cases of acute lobar pneumonia in which the capsule bacillus (bacillus pneumoniæ of Friedländer) was found in cultures of the lung together with the diplococcus lanceolatus, the growth of the capsule bacillus being so powerful that it obscured entirely the development of the diplococcus. The results of bacteriological investigation of acute lobar pneumonia at the Boston City Hospital have shown it to be due invariably to the micrococcus lanceolatus.

When in a dry state the pneumococcus retains its virulence for long periods. This is especially the case when it is protected by being mixed with mucus in desiccated sputum. Cases are on record in which the disease was communicated to newcomers in houses that had been closed for many months. Schroeder refers to a house from which thirty-two cases came to the clinic at Kiel in the course of fifteen years, one year furnishing six.[31]

According to Simon,[32] recent researches show that in fatal cases of pneumonia the specific diplococcus is quite commonly present in the blood, while in cases ending in recovery it is only exceptionally encountered. Wirtz found positive results in eighty-nine per cent. of fatal cases.

In investigations conducted at the Presbyterian Hospital, New York, the blood was examined in twelve cases of pneumonia. Two of these ended fatally, the remaining ten in recovery. In none of them was a growth of the pneumococcus obtained in the tubes inoculated with the blood.[33] The invasion of the blood usually occurs from twenty-four to forty-eight hours before death, but may be earlier or later. For prognosis this may be important. Some cases end in recovery.

With a view to ascertaining whether there was any relation between the occurrence of pneumonia after operations under an anæsthetic and the presence of pneumococci in the upper air passages before the anæsthetic was given, the writer caused a culture to be made from the fauces of each patient anæsthetized for operation at the Presbyterian Hospital during a period of several weeks. The result was that it was found to be the rule rather than the exception that the coccus was present, and this being the case no conclusion could be arrived at on the point proposed for investigation. Indeed, it was only in a very small proportion of the cases that the cultures failed to develop the pneumococcus, not enough to determine whether its occasional absence offered even the slightest immunity from operation-pneumonia, itself an infrequent occurrence.

It was next sought to ascertain whether the organism existed in the deeper air passages with anything like the same frequency as above the glottis. At my request Dr. Neumann, in the laboratory of the Presbyterian Hospital, examined the smaller bronchi in sixteen cadavers of persons dead from other diseases than pneumonia. The examinations were conducted with great care, a number of cultures being made in each case from different localities in the lungs. The result showed the presence of Fraenkel's pneumococcus in four cases and the presence of an organism resembling Fraenkel's in one case, while in eleven cases no bacilli pneumoniæ were found.

The cultures were taken from the smallest branches into which the needle could be carried.

It would seem, therefore, that while the pneumococcus of Fraenkel is very generally present above the glottis, it occurs in only from one-fourth to one-third of the cases in the deeper portions of the respiratory tract. It is an interesting question what proportion of all the cases of pneumonia is to be found in subjects whose deeper air passages are already the habitat of the specific organism.

Diagnosis.

A typical case of croupous pneumonia seen from the beginning can hardly be mistaken for any other disease. The abrupt onset, the chill, the pain, the fever, the respiration accelerated out of proportion to the pulse and temperature, and, finally, the peculiar expectoration, will suffice to establish the diagnosis even without the aid of the physical signs. But when the latter are added, and we have fine crepitation with inspiration and a little later a blowing sound with expiration, while the vocal resonance and the vocal fremitus are exaggerated, and the percussion note becomes constantly duller until it approaches flatness, there is presented a clinical picture which for vividness and individuality can hardly be surpassed.

But cases are not always seen at the outset, or accompanied by reliable histories, and we may be called upon to make a diagnosis at any stage, and with little or no knowledge of what has gone before. This is often the case in hospitals, especially in those having an ambulance service, patients being brought in in a condition of delirium, or unable from natural stupidity or from ignorance of the language to give any account of their illness. Under such circumstances we must depend largely upon the physical signs, interpreting them by such objective symptoms as may be present at the moment.

If the signs are such as have been already indicated and the temperature is high and the breathing hurried, we may be sure that we have a pneumonia which has not yet defervesced.

If with the physical signs of consolidation we have a low temperature, and the breathing is but little accelerated, and there is more or less creamy expectoration, we may assume that the case is one of pneumonia which has passed the crisis. If under like conditions we detect crepitation in the consolidated portion, we have a commencing resolution signalized by the râle redux. Finally, if we have a temperature varying but little from the normal, slight percussion dulness, vesiculotubular breathing interspersed with coarse mucous râles, and accompanied by a mucopurulent and partly frothy expectoration, the

inference is that the case is one of pneumonia pretty well advanced in the process of resolution.

We must remember, also, that not all cases of pneumonia run a typical course. There is scarcely one of the classical symptoms or signs that may not sometimes be wanting. In about twenty per cent. of all cases the chill is absent. Pain is not a marked feature unless the pleura is involved, and in central pneumonia it is often not severe enough to excite complaint. In feeble or elderly persons the fever may be slight; indeed, even apart from these conditions, some of the worst cases we meet with show but a moderate temperature throughout. The pulse is likely to correspond with the temperature; and the respiration, usually the most characteristic of the symptoms, is sometimes not strikingly frequent. Cough and expectoration may be entirely absent through the whole course of the disease, or the cough may bring up only a little frothy mucus from the bronchial tubes.

As to the physical signs, all of them may be in abeyance for a considerable time when the consolidation is confined to the central portion of the lung. A greatly thickened pleura remaining from a former pleuritis may obscure the results of both auscultation and percussion, and lead to mistaken inferences.

Apart from the above considerations the diagnosis of pneumonia involves differentiation from quite a range of affections, such as bronchopneumonia, pulmonary œdema, pleurisy with effusion, abscess of the liver, pulmonary apoplexy, pulmonary phthisis, cancer of the lung, atelectasis, engorgement in fever, typhoid fever.

Bronchopneumonia is distinguished from acute lobar pneumonia by the less frequent occurrence of chill in the former, the less degree of pain, the pain being at the same time less fixed, a generally lower temperature, less increase in the rate of respiration as compared with temperature; while the cough is more severe, and the expectoration is more abundant, more frothy, less stained, and less adhesive. The disease is more frequently bilateral in the bronchial form than in the lobar. The dulness is much less circumscribed, and is more likely to appear in several places at once, and to shift its locality from day to day. The breathing over the affected part has not the tubular blowing type of lobar pneumonia, and is relatively feebler. Fine crepitation is absent, and in its place are subcrepitant râles heard with expiration as well as inspiration. The vocal resonance and vocal fremitus are less exaggerated. In short, the physical signs indicate that the consolidation is far less perfect than in the lobar form. As the case progresses we miss the distinctive crisis, and there are not the characteristic traits of a self-limited disease. In favorable

cases amendment may begin at any time, or it may be indefinitely deferred.

According to Delafield and Prudden,[21] "there is a form of broncho-pneumonia in adults which resembles lobar pneumonia. There is a general catarrhal bronchitis, with bronchopneumonia and consolidation of one or more lobes. The symptoms and physical signs are those of lobar pneumonia, but with some difference. The invasion of the disease is not as sudden, the pulse is more rapid, the cerebral symptoms are more constant, the expectoration is like that of bronchitis, the physical signs are more slowly developed, the duration of the disease is rather longer and resolution is slower."

In pulmonary œdema we have cough, expectoration, embarrassed respiration, and some dulness on percussion. But there is no chill, no pain, no rise in temperature; the expectoration is profuse and watery, instead of small in amount and viscid. Pulmonary œdema is bilateral and begins usually in the most dependent portion of the lung, instead of being unilateral and occurring indifferently in one portion or another. In pneumonia we have the dry crepitant râle, while in œdema the râles are coarse and liquid. Bronchial breathing and bronchophony, heard in pneumonia, are absent in pulmonary œdema. Percussion dulness is less in œdema, and vocal fremitus is not exaggerated. The absence of chlorides from the urine so general in pneumonia is not observed in œdema of the lungs.

But it must be remembered that very many cases of pneumonia are complicated at some period in their course with pulmonary œdema, and we must always be alive to the possibility of the coexistence of the two affections.

Pleurisy with effusion has many points in common with lobar pneumonia. There is pain; there may be chill; there is fever; the respiration is hurried; there is a cough; and there is an area of percussion flatness. In some cases there is also bronchial breathing. When this is present the differential diagnosis may be far from easy.

But the fever is comparatively mild, the temperature rarely reaching 103° F., and the respiration does not fluctuate so widely with each change of temperature as is the case in pneumonia. There are not the nervous shock, the loss of muscular strength, the evidences of profound intoxication, seen in pronounced toxic cases of pneumonia. The cough is dry, there is but little expectoration, and what there is is frothy, not stained, not adhesive. If the effusion is considerable, the heart will be displaced towards the unaffected side.

Coming to the physical signs, we note the absence of crepitation, and generally, though not always, of bronchial breathing. On the

other hand, we have the presence in the early stage of a pleural friction sound, which is often enough found in pneumonia.

Percussion reveals an area of flatness (not dulness as in pneumonia) occupying what has been the most dependent portion of the pleural cavity on the affected side, with often increased resonance above. Sometimes the level of this area will change with change of the patient's position, but generally the fluid whose presence gives rise to the flatness is kept in place by interpleural adhesions. Over this area there is in most cases absence of respiratory murmur and of voice sounds, in place of bronchial breathing and bronchophony, though both of these are present in exceptional cases. · Even in these cases there is absence of vocal fremitus, instead of the exaggeration observed in pneumonia.

There is one sign which if present and well marked goes far towards establishing the diagnosis, and that is ægophony above the line of flatness. There is nothing in pneumonia that fully answers to this, but it is not always present in pleurisy with effusion. The latter is true also in regard to bulging of the intercostal spaces and displacement of the heart or of the liver. Yet while there is no one sign or symptom which is always to be relied upon, unless it may be the absence of vocal fremitus, it is seldom that we need remain long in doubt, and in any case the matter may be cleared up by the harmless expedient of an exploratory puncture. We must bear in mind, however, that there are instances in which both conditions are present, and also that adhesions resulting from former inflammation may bring about some very perplexing distributions of fluid in subsequent attacks.

In simple hydrothorax there is an area of flatness with a somewhat bronchial character of the breathing and voice above it, but the upper line of the flatness, which is higher behind than in front, changes when the posture of the patient is changed. Ægophony is usually well marked. There is little or no fever, and the dyspnœa is comparatively slight, even when a large amount of fluid is present.

In pyothorax the physical conditions are much the same, and there are the symptoms of pyæmic infection, including wide excursions of temperature, sweating, etc.

In *abscess of the liver* and in subphrenic abscess, the pain and the rigor, together with an area of dulness, may suggest pneumonia of the right base. But the rigor is likely to recur again and again, there is absence of the auscultatory signs of pneumonia, and though cough may be present, we do not have the characteristic expectoration. If any doubt remains it is soon cleared up by the clinical phenomena, which, as the case proceeds, diverge widely from those observed in pneumonia.

In *pulmonary apoplexy* or hemorrhagic infarct we have pain often of a very severe character, frequent respiration, cough, an area of dulness, and, perhaps, bronchial breathing. These symptoms and signs suggest pneumonia, but the onset is too sudden, we miss the chill; the temperature is less elevated; the expectoration is abundant, and consists largely of pure blood. There are coarse râles within the lungs from the first. Moreover there is usually a history of antecedent cardiac disease, or of some infection by which the formation of pulmonary emboli or pulmonary thrombi is provoked. Attention to these points will suffice to establish the differential diagnosis.

Tuberculosis.—The consolidation attendant upon tuberculous deposit, especially if pleuritic pain be present, and if at the same time the temperature be considerable and the breathing frequent, might reasonably raise the question of the existence of pneumonia, if a history of the case should not be attainable. It might even be difficult if not impracticable at once to exclude this possibility. But the difference in the character of the sputa, the different temperature curve, and the afternoon hectic in phthisis would soon lead to a correct diagnosis. Besides, if in sufficient extent to raise the question of diagnosis, there would be likely to be auscultatory evidence of the breaking down of lung tissue. It is to be borne in mind, however, that an area of tuberculous deposit may be included in one of pneumonic exudation. If doubt remain, it may be removed by microscopical examination of the sputum.

Cancer of the lung has some features in common with pneumonia. There are pain, respiratory embarrassment, and cough, with expectoration which may be more or less stained with blood or otherwise colored. The physical signs of consolidation are also present in the affected region. But the onset is gradual and the disease protracted; there is little or no fever, no chill, the pain is continuous, there is a cancerous aspect after a time, and cancerous growth is apt to exist or to be developed in other organs. Indeed, there could be but little chance of confounding the two affections unless an inflammatory process should have been set up in a cancerous lung, and the previous history should not be obtainable, conditions which I met with once in consultation, and which had given rise to a diagnosis of unresolved pneumonia.

Atelectasis gives rise to circumscribed percussion dulness, and rapid respiration, but lacks the other features of pneumonia. Besides, it is a condition found almost exclusively in infancy.

Hypostatic Congestion.—During the course of a low fever, in which the vital powers are considerably depressed, there is likely to occur

a congestion of the lungs affecting especially the posterior portion. This gives rise to some shortness of breath, cough, frothy expectoration sometimes a little bloody, mucous râles, and some degree of dulness on percussion, and might be taken for the early stage of pneumonia. But its presence in both lungs, the absence of the crepitant râle, the comparatively slight effect upon the respiration, and the history of a preceding fever which still continues, render the distinction easy.

On the other hand, it often happens that in a protracted case of pneumonia symptoms arise that very closely resemble those of *typhoid fever;* and if the progress of the case has not been followed, it is quite easy to overlook the lung condition and see only the appearances that indicate a low form of fever. Indeed, not one of these may be wanting, and it may be only because we have more than is needed to constitute a case of typhoid that our suspicion of the true nature of the affection is aroused.

Of course, mistake would be possible only in the febrile stage of the pneumonia, and then the excessive frequency of the respiration should at once attract attention. In most cases the cough and expectoration would be significant; but granting these to be absent as they might be, there would still be enough in the respiration, including the unequal movement of the two sides of the chest, to show that the lung was implicated, and to lead to a physical examination which would be conclusive. How often this examination is neglected, however, may be inferred from the annual report of the Metropolitan Asylum Board for 1897, which states that among the cases of mistaken diagnosis are found sixty-one of pneumonia erroneously included in two hundred and ninety-three cases reported as typhoid fever.[34]

The routine application of the Widal test would reduce the chances of such error to a minimum.

The following is quoted from Osler[35]:

"Nervous symptoms are more frequent in pneumonia than in typhoid, and from the onset may so dominate that the local lesion is entirely overlooked. For instance, in the case of cerebral pneumonia of children, in which the disease sets in with a convulsion, there are high fever, delirium, great irritability, muscular tremor, and perhaps retraction of the head and neck, and consequently meningitis is usually diagnosed. Cases occur in which the malady sets in with acute mania. For example, a young man behaved so strangely on the train that he was handed over to the police as a lunatic, and as he had no cough and little fever (though he complained of a pain in the side) pneumonia was not recognized for several days. Again, pulmonary features are frequently marked where the patient has delirium tre-

mens, and error is certain to occur unless it is made an invariable rule to examine the chest in these cases. Then there are cases with toxic features resembling uræmia; without chill, cough, or pain in the side the patient may develop fever and a little shortness of breath and then gradually grow dull and heavy, and within three days there may be a condition of profound toxæmmia with low-muttering delirium. In many of these cases the most characteristic symptoms of the disease may be absent, particularly the cough and the rusty sputum; but the physical signs, if they are elicitable, are well marked. Even in the gravest of these cerebral cases the crisis and the onset of convalescence may occur in the ordinary way, and the patient may pass from a condition of extreme danger to one of perfect safety."

Complications.

Strictly speaking, the complications of pneumonia are only those morbid conditions which are so associated with the primary disease as to indicate that they are dependent upon it and would not have taken place in its absence. Conditions previously existing, or that are simply coincident, cannot rightly be considered as complicating the pneumonia, though they may be complicated by it. Thus an old cardiac or renal lesion can scarcely be said to complicate a pneumonia, though its presence may very materially affect the gravity of the case. On the other hand, an acute pericarditis or nephritis occurring in the course of a pneumonia, and evidently involved with it in some sort of causal relation, would be an illustration of what strictly constitutes a complication. There are several affections which so often appear with pneumonia as to make it reasonably certain that there is a common influence at work, and this influence can often be found in the presence of the pneumococcus in the locality in question. The following tables, compiled by Dr. Howland, show the complications observed at the Presbyterian Hospital, New York.

COMPLICATIONS OF PNEUMONIA.

Out of 488 Cases.

	Number of cases.	Recovered.	Died.
Pleurisy with effusion	20	17	3
Pericarditis (acute)	6	1	5
Otitis media *	6	6	
Thrombosis of femoral vein	3	3	
Bronchitis †	13	9	4
Jaundice	2	1	1

* Otitis of catarrhal form in every case.

† These were cases complicated with well-marked bronchitis from the outset and not those merely developing signs of œdema or of the softening of resolution.

Out of 304 Cases.

	Number of cases.	Recovered.	Died.
Gangrene of leg *	1	1	
Delayed resolution	7	7	
Relapse	2	2	
Delirium tremens	11	5	6
Pyæmia	2	..	2
Abscess of lung †	1	1	
Laryngitis	1	1	
Erysipelas	2	2	
Persistent bronchopneumonia	1	1	
Acute nephritis ‡	3	2	1
Œdema of lungs §	6	1	5
Empyema ‖	10		

Pneumonia Complicated by Coexisting Diseases or Conditions.

Out of 488 Cases.

	Number of cases.	Recovered.	Died.
Chronic endocarditis	11	3	8
Cirrhosis of liver	5	..	5
Fatty liver	4	3	1

Out of 304 Cases.

	Number of cases.	Recovered.	Died.
Chronic nephritis	7	1	6
Typhoid fever	1	..	1
Phthisis	4	..	4
Pregnancy	1	..	1
Sacculated aneurysm of aorta	1	..	1
Paralysis agitans	1	..	1
Chronic bronchitis	1	..	1
Influenza	6	6	
Cystitis	2	2	
Emphysema	2	1	1
Endarteritis	1	1	

* Caused by thrombosis of anterior tibial artery.

† Recovered after prolonged convalescence.

‡ These were well-marked cases without previous nephritis and with symptoms of acute nephritis much worse than transient albuminuria.

§ These are cases of œdema developing during the course of the disease.

‖ Satisfactory data could not be obtained as to the final outcome of these patients, but it might be interesting to notice the conclusion arrived at by Dr. Hartwell in a report covering ten years. Out of 52 cases of empyema treated in this hospital 26 gave good history of previous pneumonia and 6 more gave a possible history. Out of these 26 pneumonia cases 19 recovered and 7 died. He found that children with empyema, as a rule, did very badly unless treated early by operation; with such treatment then they did well.

Pleuritis.—The complication most frequently met with in pneumonia is pleuritis. Indeed the sharp pain, which is included in the familiar picture of the stage of invasion in pneumonia, is due, not to the disease of the lung itself, but to the involvement of the pleura. When the pneumonic process begins centrally, pain at first is either entirely absent or is manifested only as a dull ache, and it does not assume its characteristic severity until the disease has worked its way to the surface and taken hold upon the serous investment of the lung. In the great majority of cases, however, the pleura is very early involved, the stitch often being the first thing observed by the patient. Usually the pleurisy is dry, that is it gives rise only to a fibrinous exudate, which appears as well upon the parietal as upon the visceral layer, and ultimately glues the two surfaces together. In a minority of the cases there is a moderate amount of serous effusion which is later absorbed. Not very infrequently the pleura becomes the seat of pyogenic infection, and empyema results. This occurs in from one to three per cent. of all cases.* The infecting organism in these cases is the pneumococcus, which has worked its way from the lung into the pleura, and which in a serous or synovial membrane is prone to excite suppuration.

Usually the empyema occurs on the same side as the affected lung, and is then of moderate severity and runs a favorable course. But it has been observed that when this complication occurs on the side opposite the pneumonia, the prognosis is much more grave. This doubtless arises from the fact that in the first case the affection of the pleura is due to simple continuity of tissue, while in the second it is excited by cocci circulating in the blood. As already shown, cases in which the blood is infested with the organisms generally do badly, and it is to this circumstance, and not to any peculiarity of the pleuritis, that the gravity of the prognosis is to be referred. In such cases other organs than the pleura are extremely likely to be involved, either simultaneously or in succession, and under the pressure of multiplied foci of infection the patient speedily succumbs.

The friction sound of the pleuritis is quite likely to be mistaken for crepitus within the lung. Indeed the similarity of sound, especially to the subcrepitant râle, is very striking. But it cannot be gotten rid of, nor its character changed, by coughing; and this is a very important test. Of course, if the rubbing can be felt as well as heard this puts an end to all question.

Bronchitis.—Next to pleuritis bronchitis is the most frequent com-

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* It occurred ten times in three hundred and four cases at the Presbyterian Hospital.

plication of pneumonia. In a considerable number of cases a bronchial catarrh precedes the pneumonic attack, and a common cold is said to have "run into pneumonia." The frequency with which persons are declared to have been "threatened with pneumonia" bears witness to the apprehension of such sequence which is rooted in the popular, not to say the professional, mind.

In a certain sense there is always a degree of bronchial catarrh in the affected portion of the lung. Invariably the mucous membrane of the tubes leading to a consolidated area is reddened by hyperæmia, and covered by a viscid mucus. Whether this is due to irritation by the sputum, or is a primary condition, in fact a part of the process deeper down in the lung, is a question to be considered. The view of the writer is that this hyperæmia marks the track down which the microbes marched to their proper field of activity in the parenchyma of the lung. Be this as it may, there is always evidence of such hyperæmia, and its products are mingled in greater or less proportion with the characteristic pneumonic sputum.

A general association of bronchitis with a form of pneumonia constitutes a disease by itself, bronchopneumonia, which has been already treated of by another writer in an earlier volume of this work.

Somewhat allied to bronchitis is the condition known as *collateral hyperæmia*, which is frequently developed in the course of pneumonia. It appears in the previously unaffected lung and consists of a more or less intense congestion. It is largely mechanical, and is the product of two factors. The first is the forcing into the sound lung of a portion of the blood which normally should have passed through the vessels of the obstructed lung. In this the right heart is the active agent. The second factor is the aspiration of an excess of blood into the sound lung by the action of the muscles of respiration. The inspiratory effort, not resulting in adequate expansion of the crippled lung, produces a condition of negative pressure in the sound one, and blood flows into the latter in consequence. This condition, however, is seldom serious except in advanced cases, when weakness and exhaustion of the right heart are a further cause for its supervention.

Bronchitis can be considered in the light of a complication of pneumonia only when in addition to the signs of consolidation over a given area there are bronchial râles scattered abundantly over both lungs.[2]

Gangrene of the Lung.—In rare instances a portion of the hepatized lung perishes, and a condition of gangrene is established. This is due to an involvement of the nutrient vessels in the process that

ordinarily interests only the functional blood supply. The precise mechanism by which the germ obtains access to a bronchial twig cannot be traced and probably is not the same in all cases. According to Osler,[23] "the gangrene is associated with the growth of the saprophytic bacteria on a soil made favorable by the presence of the pneumococcus or the streptococcus."

The extent of the gangrene will depend upon the size of the vessel at the point where infection takes place or to which the resulting thrombus extends in a backward direction.

The occurrence of this accident is marked by an intolerable fetor of the breath and in some cases by the appearance of the physical signs of a cavity. Occasionally the destruction of tissue opens a way into the pleura, and pneumothorax results.

Though a very grave complication gangrene is not by any means necessarily fatal. If the amount of lung involved be not too great, and the vitality of the patient not already too greatly depressed, a fair chance for recovery may remain.

Pericarditis.—This complication occurs in from two to eight per cent. of the cases of pneumonia, according to different authorities. It is often overlooked during life, the area of the pneumonic dulness including that of the pericardial effusion, and auscultation not being practised at the time when the pericardial friction sound might have been heard. At the Presbyterian Hospital it was made out during life in six out of four hundred and eighty-five cases of pneumonia. It is supposed to occur more frequently when the left lung is involved, and the inference is that the disease extends from the lung and pleura by continuity of tissue. More recent investigations, however, seem to show that there is no material difference in this respect. Doubtless it is more likely to be recognized during life when the pneumonia is on the opposite side, as the area of pericardial dulness in this case is not obscured by the dulness of consolidation.

It should be the rule in every case of pneumonia to examine the cardiac area at least daily. This is especially imperative when the respiratory and circulatory conditions appear out of proportion to the temperature and the nervous symptoms. Orthopnœa, in particular, suggests something more than the dyspnœa of pneumonia, and will often be found to be associated with effusion into the pericardium or the pleura.

The extreme flatness on percussion and the absence of vocal and respiratory sounds and of vocal fremitus over the effusion will generally suffice for the diagnosis. Auscultatory percussion may be of great value in fixing the limiting line between solid and fluid, a change in the character of the note occurring at once in passing from

one to the other, though to ordinary percussion there might be no appreciable difference.

When pericarditis occurs during the progress of pneumonia the pneumococcus lanceolatus may very generally be found in the effused fluid. It is frequently associated with other organisms, but under such conditions as leave little doubt that it is the determining factor.

A pericarditis occurring as a complication of pneumonia is much more likely to be purulent than when it is primary or associated with rheumatism. In such cases pneumococci may be found in the blood, and collections of pus may form in other serous or synovial cavities. Such conditions offer little hope of recovery.

Acute Endocarditis.—This affection appears in pneumonia both as an acute condition engrafted upon an old lesion, and as a fresh invasion apart from previous anatomical change. In some cases both the pneumonia and the heart affection seem to be the outcome of rheumatic poison.

It may assume the simple form with warty vegetations, or the malignant or ulcerative type with the pneumococcus as the active agent. In either case the effect of the disease is so intensified by the associated pulmonary affection that opportunity for a complete development of the clinical history is seldom afforded. This would be still more the case, were it not that the valvular trouble involves the left side of the heart, while it is the right side that has to bear the brunt of the struggle with the unfavorable pulmonary conditions.

The following case, seen in consultation with Dr. Janvrin, of this city, illustrates an acute pneumococcic infection engrafted upon an old valvular lesion:

Mr. T——, age 67, had had for years a valvular lesion, which, however, caused him no very serious inconvenience. On December 18th, 1898, after some two weeks' confinement to the house with influenza, which did not extend below the larynx, he had a severe chill, and signs of pneumonia soon developed in the right base. There was little cough and no expectoration. Chills recurred at irregular intervals thereafter, and not yielding to quinine and arsenic, the suspicion gained ground that they were of mycotic origin, which suspicion was soon confirmed by the occurrence of murmurs indicating a fresh endocarditis. Meanwhile the pneumonia cleared up very kindly, perhaps assisted by the massive doses of quinine. But the chills, perspiration, and extreme prostration persisted with increasing severity, and death took place on the seventeenth day of the attack.

Although an autopsy could not be obtained, there can be no doubt

that the organism which excited the endocarditis in this case was the pneumococcus. Drs. Janeway and Armstrong, who also saw the case, concurred in the diagnosis.

Chronic Endocarditis.—This is not properly a complication of pneumonia, but rather a preëxisting condition. At the Presbyterian Hospital, New York, of four hundred and eighty-eight cases of pneumonia eleven occurred in persons already having chronic valvular lesions. It is a very serious combination in view of the embarrassment of the circulation which it involves. Indeed, if the leakage is considerable, or the compensation defective, the chance of recovery is very small. Of the eleven cases above referred to eight proved fatal. A chronic valvular lesion is also important as affording a possible seat for an acute infective process, as in the case just cited.

Myocarditis as an actual complication of pneumonia can very seldom be substantiated. The high temperature to which cardiac degeneration is so often attributed is not often of sufficient duration in pneumonia to bring about this result. But pneumonia may attack a person who already has a softening of the cardiac walls, and in such a case the crippling of the heart adds greatly to the danger of heart failure or, at least, of hyperæmia and fatal engorgement of the lung.

In the absence of a previous history of recognized cardiac weakness it may not be easy to say whether a softening of the myocardium, found post mortem, existed before the pneumonia or was induced by it. But we may be aided in our judgment by the character of the heart beats in the early stage of the attack, as well as by the degree and duration of the temperature.

Parotitis occurs in a small proportion of cases of pneumonia either during the course of the disease or as a sequel to it. It is rarely seen in young or vigorous persons, but belongs to the later period of life, or to conditions of depressed vitality. In all probability it is the result of microbic invasion by way of the parotid duct. It nearly always eventuates in suppuration, and it resembles the parotid abscess which occurs in typhoid fever.

It is a very serious complication both because of its occurrence in enfeebled persons, and because of the somewhat formidable character of the affection itself. It more frequently affects only one of the glands, which fact points rather to a local than a general source of infection as above indicated.

Diarrhœa is occasionally met with in the course of pneumonia. In some cases it seems to be one of the results of the first shock of the infection. In others it occurs at a later period, and may be due to the resorption of the exudate, inasmuch as it continues after the

crisis. Doubtless the cause lies in many instances in excessive feeding under conditions very unfavorable to proper digestion. It is seldom a serious complication.

Jaundice is an infrequent complication. It was noted in two cases out of four hundred and eighty-eight at the Presbyterian Hospital, though other observers have met with it in a larger proportion of cases. The precise conditions upon which it depends have not yet been decided. It is not attended by the evidence of obstruction, and is probably the direct effect of the specific poison acting upon the liver. It is usually slight and of no practical significance. Occurring, however, in a patient already having a fatty or cirrhotic liver it is of more serious import. It is sometimes associated with gastroduodenitis.

Otitis Media.—This occurred six times in four hundred and eighty-eight cases at the Presbyterian Hospital. In all these cases it was of the catarrhal variety and ended in recovery. Purulent otitis media, however, is occasionally met with, and in these cases the pneumococcus may usually be demonstrated in the pus. It is fair to presume that the coccus finds its way into the middle ear through the Eustachian tube. The purulent form adds a considerable element of danger to the existing pneumonia.

Neuroses.—Among the neuroses complicating pneumonia Isager[36] observed aphasia in a boy nine years old. The aphasia was complete, the boy being unable to speak though understanding what was said. After a fortnight the aphasia gradually disappeared.

Leszynsky[37] presented a man before the New York Neurological Society suffering from neuritis of the brachial plexus which had come on in the course of pneumonia.

Voute, of Amsterdam,[38] observed external oculomotor paralysis arising in a case of apical pneumonia, the paralytic symptoms subsiding as resolution took place. He considered the paralysis to be of toxic origin rather than meningeal, as there was complete absence of cerebral symptoms.

Pregnancy.—The existence of advanced pregnancy adds greatly to the seriousness of an attack of pneumonia. The interference with respiration occasioned by the upward pressure is a matter of grave moment. In addition to this, premature labor is very likely to occur, imposing a heavy tax upon the already overburdened system. In the early months the danger is much less. Should the life of the fœtus be destroyed at this stage of the infection the abortion may be delayed sufficiently to give time for recovery from the pneumonia. An interesting case is reported by Verlet[39] in which a pregnant woman was attacked with pneumonia followed by a relapse. Premature de-

livery resulted, the child born at seven months was cared for in an incubator, and both mother and child did well.

Venous Thrombosis.—Thrombosis of the femoral vein is met with not very infrequently. Three cases are recorded in the four hundred and eighty-eight mentioned above. Increased fibrinosis seems to be a characteristic of the pneumonic state, and probably this condition lies at the bottom of the coagulation in the vessels. As in thrombosis from other causes, the left leg is more frequently affected than the right.

Da Costa[40] in a clinical lecture refers to three cases of this kind which have occurred in his practice. I saw a similar case in private practice some years ago. The vein remained occluded years afterward, and the limb became swollen after much standing or walking.

In the treatment of recent cases of thrombosis local frictions should be carefully avoided lest the clot be dislodged and carried into the circulation. Clots may be formed in the vessels of the interior, and doubtless many of the cases of sudden death observed in pneumonia are due to their translation into the pulmonary veins.

Meningitis.—Diplococci have been reported as found in the pus of meningitis by many bacteriologists, and these organisms have been frequently and fully identified as "diplococcus pneumoniæ." Netter, in 1889, in a report of 25 cases of purulent meningitis, states that 13 of these were examined microscopically, by cultures, and by inoculations into animals, 6 microscopically and by experiments on animals, and the rest microscopically only. Six of the cases were complicated with pneumonia, 4 with purulent otitis, and 3 with ulcerative endocarditis. In 16 of the 25 cases the pneumococcus was found; in 4 the streptococcus pyogenes, in 2 the diplococcus intracellularis meningitidis of Weichselbaum, in 1 Friedländer's bacillus, in 1 Newman and Schaffer's motile bacillus, and in 1 a small curved bacillus. Out of 45 cases gathered by Netter, this micrococcus was found in 27; streptococcus pyogenes in 6; and the diplococcus intracellularis meningitidis of Weichselbaum in 10.

In 4 cases of cerebrospinal meningitis, reported in 1889, Monti demonstrated the presence of this micrococcus in 3 of which pneumonia was a complication. In 2 cases the staphylococcus pyogenes aureus was present with the diplococcus pneumoniæ. Weichselbaum, in 29 cases of ulcerative endocarditis examined in 1888, found the diplococcus pneumoniæ in 7.

Testi in 1889, in a case of parotitis complicating lobar pneumonia, obtained the micrococcus pneumoniæ crouposæ from the pus in pure cultures, and in another case of pneumonia complicated with a purulent pleuritis, bilateral parotid abscess, and multiple subcuta-

neous abscesses, the pus from these varied sources all contained the diplococcus in large numbers. This was shown by microscopical examination and by inoculation into rabbits. Gabbi (1889) obtained the same coccus in pure cultures in a case of tonsillitis resulting in abscess.

In a considerable number of cases of otitis media this micrococcus has been found, and in pus secured by paracentesis of the tympanum, and frequently in pure cultures; by Zaufal (1889) in 6 cases, Levy and Schraeder (1889) in 3 out of 10 cases in which paracentesis was performed; by Netter (1889) in 5 out of 18 cases occurring in children. In 1889 Monti and Belfanti both reported cases of arthritis of the wrist-joint complicating pneumonia, in which this micrococcus was found in pure cultures. Ortmann and Samter in the same year obtained the diplococcus pneumoniæ in pure cultures in a case of purulent inflammation at the shoulder-joint following pneumonia and pleurisy.[12]

Prognosis.

The prognosis in pneumonia is modified by a number of preexisting conditions, the principal of which are sex, age, season of the year, habit as to the use of alcohol, and the presence or absence of certain chronic diseases.

It is conceded that while pneumonia occurs more frequently in men, it is more fatal in women. Of 223 patients with pneumonia admitted into the Presbyterian Hospital, 170 were males, with a mortality of 28.8 per cent., and 53 females, with a mortality of 31.2 per cent.

PNEUMONIA—434 CASES.

Relation to Age.	Died.	Percentage dying.	Recovered.	Percentage recovered.
Below 5 years..............	0	0	13	100
Between 5 and 10 years.....	0	0	18	100
" 10 " 15 "	1	9	11	91
" 15 " 20 "	7	23 +	23	76 +
" 20 " 30 "	28	22 +	95	77 +
" 30 " 40 "	37	37 +	62	62 +
" 40 " 50 "	31	42 +	42	57 +
" 50 " 60 "	16	47 +	18	52 +
" 60 " 70 "	16	66 +	8	33 +
Over 70* years..	5	62 +	3	37 +
	141	32 +	293	67 +

*It is not to be inferred, however, that the increased mortality as age advances is due entirely to senility. The greater frequency of preëxisting morbid conditions comes into the reckoning. The man of sixty has had two chances to contract bad

Before the age of two years lobar pneumonia is a rather rare disease. After that age the mortality is greater in proportion as the patient is older. The preceding table, based upon four hundred and thirty-four cases treated at the Presbyterian Hospital, New York, shows not only the frequency of occurrence, but also the mortality at the different ages.

Statistics accumulated by Frankel and Reiche (Maragliano[41]) covering 1,130 cases give the mortality by ages as follows:

From 1 to 5 years	30.0	per cent.
" 6 " 10 "	3.84	"
" 11 " 20 "	10.05	"
" 21 " 30 "	8.70	"
" 31 " 40 "	24.70	"
" 41 " 50 "	39.30	"
" 51 " 60 "	43.10	"
" 61 " 70 "	63.60	"
" 71 " 80 "	86.70	"

The relative mortality of pneumonia in the different seasons of the year is variously stated by different writers. In the above two hundred and twenty-three cases, the spring months gave the lowest mortality, the summer showed a slight increase, while in the autumn and winter the death rate attained its highest percentage.

The habitual abuse of alcohol unfits the system to bear up against pneumonia. Of 11 such cases, referred to by Ewing as occurring at Roosevelt Hospital, only 3 recovered. The records of the Presbyterian Hospital covering 428 cases give the following results as to mortality among those markedly alcoholic, those moderately alcoholic, and those non-alcoholic.

PNEUMONIA—428 CASES.

Relation to Alcoholism.	Died.	Percentage dying.	Recovered.	Percentage recovered.
Markedly alcoholic *	36	70	15	29
Moderately alcoholic	52	32	109	67
Non-alcoholic	45	20	171	79

A preëxisting rheumatic habit has generally been observed to add to the gravity of the prognosis. It was present in 20 of the 223 Presbyterian Hospital cases and was attended by a mortality of 40 per cent. As the rheumatic habit, however, is more pronounced as

kidneys for one chance that has come to the man of thirty; and so through all the list of chronic diseases whose presence renders an attack of pneumonia more perilous.

* A noticeable fact was that of the fifteen recoveries, most of them were in young men between twenty and thirty years.

life advances, the influence of age in these cases must not be overlooked.

The prognosis is extremely unfavorable in diabetic patients. The combustion of the sugar, already imperfect, is diminished in proportion to the impairment of the respiration. Death in such cases is preceded by delirium and coma.

The preëxistence of chronic nephritis makes the prognosis of pneumonia more grave in proportion to the renal insufficiency and the accompanying cardiovascular changes.

Pneumonia occurring in a subject of advanced cardiac disease is likely to prove fatal. The prognosis is less grave before secondary changes have taken place in the right side of the heart.

Coming now to the conditions arising in the course of the disease, and which seem to influence the mortality, the first is the initial chill. This occurred in 144 out of the 223 cases, with a mortality of 34 per cent., while the remaining 79 cases in which the chill was absent gave a death rate of only 19 per cent. From this it is evident that the chill is an expression of a severer grade of infection, and I have observed that usually a prolonged rigor with tardy reaction presages an unusual degree of muscular and nervous prostration.

The prognosis depends largely upon the extent of the pneumonia. When both lungs are involved not half of the patients recover. Pneumonia occupying the whole of a lung is more dangerous than when only a part of the lung is involved.

As to the location of the lesion, the right lung is more frequently affected than the left, and also gives a higher mortality. Of 94 cases implicating the right lung alone, 28 ended fatally, giving a mortality of 29.8 per cent., while only 62 cases involved the left lung alone, of which 16, or 24.5 per cent., were fatal. In 39 cases both lungs were involved, with a mortality of 19, or 48.7 per cent. Previous attacks do not affect the prognosis.

A feeble pulse that is frequent in relation to the respiration and temperature has much the same prognostic significance as a heavy and prolonged chill. In my experience it indicates a profound specific infection, that is likely to carry off the patient at or before the crisis.

The respiration is always frequent in pneumonia, but when extreme frequency is associated with a high temperature, it has less significance than when it occurs without this association. In the former case it is due in part to the fever; in the later it denotes extensive lung implication, and probably œdema, always a perilous condition.

Up to 105° the danger does not seem to increase materially with

the rise of temperature. Thus in 45 cases with the maximum temperature ranging between 100° and 103° the mortality was 26.6 per cent., while in 99 cases with temperature between 103° and 105° the mortality was 26.3 per cent. The conditions that raise the temperature above 105°, however, immediately tell upon the death rate. In 49 cases with a temperature between 105° and 106° the mortality was 32.1 per cent., and 13 cases at 106° and upwards gave 61.5 per cent. of deaths. Recovery, however, may take place though the temperature attain an extraordinary height. Wagner has reported such a case in a boy five years old, the temperature having reached 109.2° F. Indeed, it is an error to attach too much importance to the temperature alone, so long as the condition otherwise remains favorable. Measures intended merely to control the pyrexia are indicated only in extreme cases. It cannot be too often repeated that to give coal-tar preparations according to indications furnished by the thermometer is to expose the patient to a real danger in an effort to rescue him from a fancied one.

There is a physical sign to which I called attention some years ago that I regard as important in the prognosis of pneumonia, and to which I have already referred in another connection. This is the character of the valve sound heard in the pulmonary area. The resistance in the pulmonary circulation which always exists in these cases must necessarily increase the tension in the pulmonary artery, provided the force of the ventricular systole is not impaired. With this increased tension come a sharper recoil of the blood against the valve cusps and a greater intensity of the valve sound. It follows, other things being equal, that in this intensity we have practically a measure of the degree of obstruction to the blood current in the lungs.

It is generally very easy to note as consolidation progresses the constantly increasing sharpness of the pulmonary second sound, and in favorable cases this accentuation, after reaching a certain point, is maintained with little change until commencing resolution renders the circulation easier, when the valve sound loses in intensity in proportion as the pulmonary condition improves.

But, unhappily, loss of accentuation of the pulmonary second sound does not always depend upon relief of the pulmonary circulation. It may signify instead a weakening of the right ventricle and a lessened power to force the blood into the artery. This comes when the right heart begins to flag either from exhaustion from excessive labor, or because of the depression arising from the specific infection. In either case, when we find the pulmonary second sound becoming weaker without any evidence of a favorable change in the condition

of the lung, we may draw the conclusion that the right heart is failing, and that the tendency of the case is towards a fatal termination.

The information furnished by the pulmonary valve sound is much more reliable than that supplied by the radial pulse, for in most cases the chief peril is of failure of the right heart from exhaustion, and of this the condition of the radial pulse will give only indirect and inconclusive evidence. The right ventricle may be on the verge of exhaustion, while the left retains almost undiminished vigor, and the radial pulse then will simply indicate that less blood than usual is flowing beneath the finger, as the result of paucity of blood in the left ventricle.

Unfortunately it will sometimes happen that the region of the pulmonary area is occupied by noisy râles, so that it may be difficult or perhaps impossible to appreciate the action of the valve. But unless the dyspnœa is extreme the breath can be held for an instant, and for the practised ear the briefest moment is sufficient. An emphysematous condition of the left apex may also obscure the sound of the valve or render it inaudible.

As to the prognostic value of the data furnished in this way, I can only say that I have never seen disaster come in a case of pneumonia unless it was preceded by a period in which the pulmonary valve sound was progressively losing in intensity. Or, to put it in other words, I have never seen a case with sharp and distinct pulmonary valve sound in which a favorable prognosis as to the immediate future was not justified by the event. The weakness of the right heart that is indicated when the valve sound becomes less intense takes place chiefly in two classes of cases. The first is that in which the system is overwhelmed by the virulence of the infection. These cases are marked by a severe and protracted initial chill, great muscular prostration, a small and relatively frequent pulse, and marked involvement of the nervous system. We may well believe that in such cases the heart muscle is poisoned, and that consequently the right ventricle with the increased labor thrown upon it early becomes exhausted. Such cases are apt to prove fatal before defervescence takes place. If they can be carried beyond this period the prognosis is greatly bettered.

The second class of cases is made up of those in which from age, intemperance, previous illness, or other cause, the integrity of the circulatory apparatus is compromised in advance. Here we have a constant tendency to the invasion of fresh areas of lung, and to the supervention of œdema. This tendency, while it increases the labor required of the ventricle, is itself increased in proportion as the ventricle weakens under its burden.

The exact relation between the temperature and leucocytosis in pneumonia is not yet fully determined; but in general terms it may be stated that a high temperature in a vigorous subject carries with it a large number of leucocytes. From a prognostic point of view this is of great importance. Whether we consider the leucocytes as scavengers, and assume that they destroy the cocci which are the medium of infection, or whether we assign to the white cells a share in the production of antitoxin, certain it is that severe cases in which there is marked leucocytosis do better, as a rule, than similar cases in which the increase of white cells is relatively slight.

When the leucocytosis is inconsiderable it will generally be found that the system is not reacting energetically against the infection, a condition which suggests an unfavorable prognosis.

On the other hand, there may be a high degree of leucocytosis which is not due to the pneumonia pure and simple, but to some complication as pleuritis or pericarditis, and if this is not taken into account a faulty prognosis may result.

Ewing, in an excellent article on this subject,[41a] gives the count of the white cells in 101 cases, of which 37 were fatal. He says: "An examination of the deaths will show that in severe forms of lobar pneumonia a slight leucocytosis is a very unfavorable sign. In 6 fatal cases the number of leucocytes was subnormal. In 11 cases the average number was 9,000. Not one case recovered, in which the disease was even of moderate severity, when the number of leucocytes fell below 14,000. In several instances, again, a slight leucocytosis seemed at the time the only unfavorable prognostic sign in cases ending fatally."

M. Laehr,[41b] in an article on "Leucocytosis in Pneumonia," published in 1893, maintains that in pneumonia there is an unmistakable connection between the temperature and the leucocytosis. When the disease is at its acme the count of the white cells is at the highest, while at the crisis there is a falling-off. In pseudo-crisis and deferred resolution the leucocytosis continues though the temperature falls. In the generally constant agreement of the course of the fever, the amount of the lung infiltration, and the leucocytosis, the author sees a dependence upon a fourth factor, viz., the intensity of the infection, that is, the quantity and quality of the bacillus poison and the power of reaction of the individual. He goes on to say: "Still more important is the prognostic significance. If the number of leucocytes does not fall with the decline of the fever we may conclude that the process has not yet arrived at a standstill. If it falls with the fall of the temperature, but rises again the following day, we must be pre-

pared for a renewed attack of the fever or the occurrence of some form of complication."

R. C. Cabot[42] gives the count of the white cells in 49 cases of pneumonia. Leucocytosis was present in 41 cases with 10 deaths; absent in 5 cases with 5 deaths; doubtful in 3 cases with 2 deaths. He says: "So far as these figures go, therefore, it would seem that while the presence of leucocytosis is not a very hopeful sign, its absence makes the outlook bad. Moreover, in two of these five cases the other reasons for giving a bad or guarded prognosis were not present. The individuals were both under fifty, were not at all alcoholic or weakly, and there was nothing in the condition of the pulse, temperature, or physical signs in the chest to lead one to expect a fatal result. Yet both went down with surprising rapidity, and without any reaction to vigorous stimulation and supportive treatment."

In a subsequent paper[43] he adds twenty-four new cases, without materially changing the conclusions to which his figures would point.

Regarding this subject Dyce Duckworth[44] concludes that both clinical inquiry and laboratory experiments have shown that leucocytosis is usually a favorable sign in pneumonia. This is well established by the observations of von Limbeck, Billings, and others who find that an active inflammatory leucocytosis during fever usually indicates a good reaction and while not invariably so, is often a good prognostic sign. The cells increased in number are the multinuclear or neutrophile, or finely granular eosinophile cells. Conversely, absence of leucocytosis is, in any case, usually a bad omen. Kanthack and Lloyd declare diminished leucocytosis with falling temperature to be a favorable sign, while a continuous high temperature with a small number of leucocytes is unfavorable. They also noticed that a persisting or increasing leucocytosis with fever is favorable. A satisfactory prognosis is not established by the presence of leucocytosis, but it is a most valuable indication when taken with associated temperature, the curves of which are often roughly parallel. Kanthack and Romer confirm these views through experiments upon animals, since they found that on injecting pneumonic bacterial toxin, if recovery took place, there was at first a sudden decrease in the number of leucocytes, followed by a rapid increase together with fever, and again persisting leucocytosis, with a gradual disappearance of the excess of leucocytes as the temperature fell. When a fatal dose was injected, the leucocytes diminished in number, and continued so, while the temperature became subnormal.

A remarkably high leucocytosis, especially if associated with a low temperature, suggests a suppurative complication. Thus in a case of pneumonia at the Presbyterian Hospital the temperature of

the seventh day was 103°, and the count 54,500. The crisis occurred the next day, but with a temperature of only 99° F. there was still a leucocytosis of 42,000. Examination showed that an empyema was developing. In another case with a similar complication the count was 44,000, while the temperature was 101.3°. In eight uncomplicated cases the highest in eighty-one daily counts was 41,000.

At the Presbyterian Hospital, in cases in which we wish to follow the leucocytosis from day to day, we have adopted the plan of recording it on the temperature chart, allowing for each additional 3,000 leucocytes a space on the chart equal to one degree of temperature. Regarding 9,000 as the normal, this figure would correspond with the normal temperature line; 13,000 would be recorded on the 100° line; 16,000 on the 101° line; 19,000 on the next line above; and so on, the tracing being done in red ink (in the accompanying chart [No. 3, page 28] in dotted line.) In this way the relation of the count to the temperature is apparent at a glance.

Much has been said regarding the prognostic significance of herpes labialis, an affection that occurs very frequently in the course of pneumonia. The general opinion is that it is of good augury, though why it should be so is not easily explained. Tallman,[45] however, concludes that it is due to individual peculiarity, many persons having outbreaks at other times and, therefore, being liable to an attack during pneumonia. It is not critical and may appear early or late indifferently. It is not coincident with a fall of temperature or a change in the general or local conditions. Its prognostic significance is generally, though not always, good. Germain Sée observed a mortality of 9 per cent. in cases with herpes as against a mortality of 25 to 30 per cent. in general.

Dyce Duckworth[44] considers that it is a good sign and usually accompanies cases in which a well-defined crisis occurs on the sixth day. Cases that are grave and those that are prolonged with deferred crisis, usually do not present it. He says further that a good sign, even in a lean and elderly patient, is an abundant rusty sputum with a fresh bright color. But when the sputa are of a "green-gage" color or bistre tint the augury is not good, and sputa of a dirty orange color are of distinctly unfavorable prognosis. The prognosis in Bright's disease is grave and indications of dextrocardiac distention and general cardiac failure are invariably serious. Favorable symptoms at the crisis are sweating and some diarrhœa.

According to Loomis,[1] the appearance of prune-juice expectoration is an unfavorable symptom, as it indicates a depraved condition of the blood. If there is an absence of expectoration in the second and third stages or if the expectoration becomes scanty and difficult

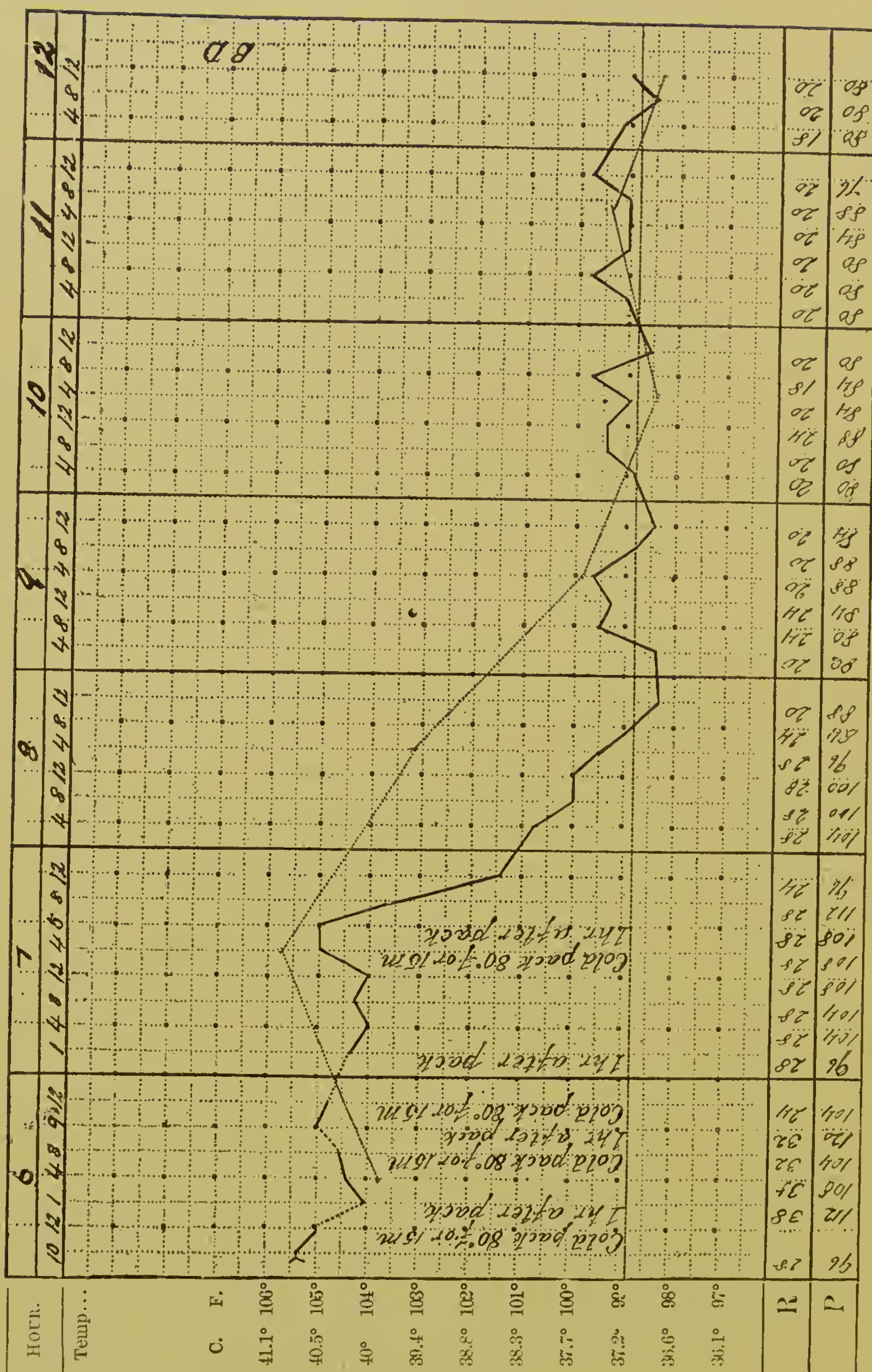

CHART No. 3.—The patient entered hospital on the sixth day of the disease with a temperature of 105.5°; highest leucocytosis on the seventh day, 29,000; normal temperature by crisis on the eighth day; normal leucocytosis on the tenth day.

the outlook is grave. Any sudden cessation of expectoration at any stage of the disease, if accompanied by tracheal râles, indicates the near approach of death. Delirium is an unfavorable sign except when it occurs early in the disease.

In the aged a sudden rise or fall of temperature, apathy, somnolence, and a sallow complexion, are all indicative of great danger.

The mortality in pneumonia varies enormously under different conditions. It is much greater in hospitals than in private practice, and in civil than in military hospitals. In civil hospitals the patients are usually taken from a class of persons imperfectly nourished, under bad hygienic conditions, and often with impaired constitutions as the result of these conditions. Then, too, only the very worst cases are sent to hospitals, the milder ones being treated at home. Add to this that the hospital patients as a rule do not present themselves until the disease is far advanced, and that they are subjected to the exhaustion due to removal, and it is not remarkable that the death rate in such institutions is very high. Of the last 458 cases treated at the Presbyterian Hospital 154 terminated fatally, being about 33.2 per cent.

Osler[46] gives the mortality in eight large hospitals as follows: Montreal General Hospital, 20.4 per cent.; Massachusetts General Hospital, 25 per cent.; Charité New Orleans Hospital, 38 per cent.; Boston City Hospital, 29.1 per cent.; Pennsylvania Hospital, 29.1 per cent.; St. Thomas', London, 20 per cent.; St. Bartholomew's, London, 18.6 per cent.; Edinburgh Royal Infirmary, 28.8 per cent.

This gives an average of 26.1 per cent., which pretty fairly represents the result of hospital practice. The greater mortality at the Presbyterian Hospital is due to the ambulance service, which brings in many patients who are practically moribund on admission.

In military hospitals, where the patients are young, vigorous males, and are admitted at the first moment of the attack, the mortality ranges from 3½ to 7½ per cent.

In private practice the conditions are for the most part the reverse of those obtaining in civil hospitals, and the mortality is proportionately less. For obvious reasons it is not practicable to accumulate accurate statistics, but the general fact is patent to every practitioner.

There has been for the last few years a very general impression in the minds of the profession that the death rate in pneumonia in this country had rather increased than diminished during the last two or three decades. Statistics gathered by Dr. Coolidge, of Boston, seem, however, to refute this idea.

Epidemics of pneumonia differ greatly in the death rate which

attends them. The same is true of different years and different localities, even when no epidemic influence appears to be prevailing. There are epidemics in which a large number of persons are affected, but the mortality is small. In other epidemics "almost every person is doomed" (Wells[18]). In certain years nearly all the cases in a given locality terminate favorably, while in other years in the same locality the mortality is very great.

These facts can scarcely be explained except on the assumption that there is a difference in the microbe at different times and in different places, similar to the differences existing in the cultures obtained in the laboratory.

These variations in the type of the disease probably afford the explanation of the phenomenal success of given forms of treatment in the hands of certain practitioners, and their utter failure when employed at other times, and in other places, and by other practitioners. They should warn us not to accept too readily the enthusiastic praises of particular methods (backed up it may be by an array of favorable statistics) which are passing in constant procession through the medical periodicals. It has happened to most of us, no doubt, to have had a succession of favorable cases under a particular management, until we came to believe that at last we had learned how to treat pneumonia. But just as we were beginning to rest in this assurance, we have been chagrined by encountering an equal array of failures with our trusted method, and have been ready to conclude that all treatment was of doubtful value. The lesson to be learned is, that an intelligent application of principles is to be aimed at, rather than a search for some particular method or formula.

Etiology.

While the essential cause of pneumonia is the development of a specific germ in the pulmonary alveoli, it is evident that as a rule there must be a contributing cause that in some way lays the system open to attack. We know that the pneumococcus is present in the upper respiratory tract in very many persons in perfect health, nay more, that it may be found in the blood, and even may be the pyogenic agent in a meningitis, a pleuritis, or a synovitis, and yet the lung escape. We must therefore assume that in any given case there is a condition present that favors either the migration of the germ into the lung or its development when there, or both.

Some of the causes that bring about this condition we are able to recognize, though we may not be able to trace their mode of action.

Sex seems to be a predisposing cause, since males are more fre-

quently attacked than females. That this is not due wholly to difference of occupation and habits, but partly to difference of structure or of constitution, is shown by the fact that in infancy boys are more frequently attacked than girls. Men are more exposed than women to cold and dampness and to excessive and exhausting labor, all of which increase the liability to pneumonia. Intemperance, too, is more common among men and adds greatly to the risk.

The relative frequency in the two sexes is variously stated; Wells,[18] from an analysis of 33,606 cases, gives 23,853 as occurring in males, and 9,753 in females. In 223 cases at the Presbyterian Hospital, in New York, the figures were 170 and 53 respectively.

Age.—Considering the total number of persons living at any given age, it is probable that the ratio of cases in successive decades is fairly uniform, except during the most active period of life, when exposure is greatest. Senility can scarcely be said to increase the liability to attack, though it adds immensely to the danger if an attack occurs.

Race.—In America, the negro race seems to be decidedly more liable to pneumonia than the white. This is clearly shown by the statistics of the Southern States, and also by the reports of army medical officers in the charge of colored troops. In the latter case it cannot be due to difference in mode of life, as the conditions are absolutely the same for all soldiers irrespective of color. It is doubtless only a manifestation of the peculiar delicacy of the respiratory organs characteristic of the negro when removed from the original habitat of his race.

Former Attacks.—Unquestionably a person who has passed through one attack is more liable to incur another. Instances are cited in which as many as eight or ten or even more attacks have been recovered from. In such cases it is probable that a bacterial residuum remains from one seizure to the next.

Unsanitary Living.—Pneumonia occurs more frequently in crowded, dark, and ill-ventilated dwellings than where the supply of light and air is ample. The life of the tenement house is peculiarly favorable to its development, and the crowded, stuffy, overheated workshop is responsible for an undue proportion of cases. Fortunately the germ is short-lived, or the disease would become endemic in such locations. As it is, the conditions render the lungs especially vulnerable to the action of the specific organism and increase the chances of infection.

Such being the principal predisposing causes of pneumonia, we have now to consider those which appear directly to determine the attack.

The first, and by far the most frequent, is *exposure to cold*. The connection between such exposure and the subsequent attack is often too direct to leave any doubt of the causal relation. For example, of persons rescued after falling into very cold water a considerable proportion will have pneumonia, and that without having been submerged or having taken water into the air passages. But even comparatively slight chilling of the surface, especially if continued for a considerable time, is very frequently followed by an attack which may, or may not, be preceded by the usual symptoms of a cold. A period of unusually low temperature very generally leads to an increased prevalence of pneumonia, especially among young children and aged people. The former for the most part get well, but after a long cold snap there is pretty certain to be a notable increase in the obituary notices of old people, most of whom will have died of the disease in question. How it is that this impression of cold brings about the specific disease in the lung we do not really know. It may be that the temporary arrest of the function of the skin causes a retention of excrementitious matter in the blood, which, seeking elimination through the lungs, determines there a local irritation favorable to the development of the germ. Or the constringing effect of cold upon the cutaneous vessels, by forcing the blood back upon the internal viscera, may induce such a congestion of the pulmonary capillaries as to favor the initiation of a pathological process. A chilling of the surface is very generally attended by a sense of discomfort in the lungs which warns us that we are in danger of "taking cold."

To this may be added a dryness of the bronchial mucous membrane, which, by impairing the action of the cilia, deprives the deeper portion of the lung of the protection that the ciliary movement affords against the invasion of harmful particles, the pneumococcus included. And, lastly, it may be that cold occasions a general lowering of the system, making it an easier prey to morbific influences. This last is the explanation usually given, but it is difficult to understand how such a degree of depression should be so quickly induced, and why it should not manifest itself in other ways as well, and also why much greater depression produced by other causes does not have pneumonia as a result.

While in a large proportion of hospital cases the disease is found to have followed upon a debauch, we are not warranted in assuming that intemperance as such is a cause of pneumonia. But it so often leads to exposure, and so generally interferes with regular and proper living, that its victims are always the subjects of impaired vitality, and therefore especially liable to this disease.

While it is popularly believed that a common acute bronhialc

catarrh may "run into pneumonia," there is no clinical evidence of such a tendency. When pneumonia occurs it is very rarely preceded by bronchitis or other pulmonary affection, and the presence of such a condition does not expose to greater risk of pneumonia. Even tuberculous subjects are not for that reason more likely to contract the affection, and it is just as likely to seize upon another portion of the lung as upon the seat of tuberculous deposit. On the other hand, pulmonary emphysema and asthma seem to confer some degree of immunity against pneumonic attacks. Flint thinks that this is true also of valvular disease of the heart.[66]

Other infectious diseases seem often to open the way to infection by the pneumococcus. The specific fevers, typhus and typhoid, measles, erysipelas, dysentery, each is a frequent forerunner of pneumonia, and holds a causal relation to it. In these cases the pneumonia is modified by the preëxisting disease, and seldom follows the regular clinical course. It is apt to assume a wandering form, appearing in patches in different parts of the lungs, presenting irregular and fluctuating temperatures, lacking a definite crisis, etc.

The morbidity varies considerably with the different *seasons* of the year. According to Flint,[47] the period of greatest frequency is during the spring months, the winter months come next, while the period from June 1st to December 1st affords the smallest number. This corresponds with observations at the Presbyterian Hospital in New York.

In reference to *climate*, pneumonia occurs more frequently in the southern portion of this country than in the Northern States, where the air is colder, and the conditions are apparently more favorable for its development. Thus it is evident that it is not a question of temperature, but of some other influence, the nature of which is not yet understood, but which probably has a relation to the life history of the specific microbe.

The frequency of the disease at the same season of the year and in the same locality varies greatly in different years.

Pneumonia sems to be more prevalent in high altitudes than at places nearer the sea-level. The epidemics of pneumonia occurring in Switzerland are mostly confined to the high valleys, while the reverse is true with regard to epidemic catarrh.[48]

Arthur Trower[49] mentions a case of septic pneumonia in a patient who had suffered from spinal paralysis for three years and was in feeble health. The sepsis apparently resulted from the pressure of, and inattention to, a dental plate that had not been removed for several weeks. Upon its removal a gangrenous condition of the mucous membrane of the hard palate was discovered, and the continuous

inhalation, swallowing, and absorption of the poison was the undoubted cause of the pneumonia.

Kronig[50] insists that it is dangerous to place a patient with pneumonia near one suffering from tuberculosis, as the latter infection is peculiarly liable to engraft itself upon the former.

Post-Operative Pneumonia.—The use of anæsthetics by inhalation in surgical operations seems to be occasionally the cause of pneumonia. Silk quotes Cheevers as giving pneumonia a prominent place among the causes of death after operations. This was in 1843, before the days of anæsthesia. In Cheevers' paper are given some observations of Erichsen, showing that of forty-one deaths after surgical injury no less than twenty-three subjects presented signs of pneumonia. In contrast to this, modern surgery, as shown by Silk presents only one case in 5,000 operations.[51] Prescott, on the other hand, estimates that in 40,000 cases of etherization there were only 3 cases of acute lobar pneumonia.[52]

At the Presbyterian Hospital, New York, in the ten years from 1887 to 1897, there were 4,914 administrations of ether followed by 17 pneumonias, 9 of which were fatal; 689 administrations of chloroform with 8 pneumonias, 7 fatal; 116 administrations of ether and chloroform with 2 pneumonias, both fatal.

It will be seen from these figures that pneumonia after anæsthesia is much oftener fatal than under other conditions, and that the administration of chloroform is much more likely to be followed by a fatal attack than when ether is employed. Schultze, however, from whose report the above statistics are taken,[53] does not believe that this large mortality following chloroform inhalation is due to the anæsthetic chosen so much as to the fact of the great number of cases of malignant disease of the mouth or respiratory tract among those to whom chloroform was given.

Of the cases at the Presbyterian Hospital 18 occurred in males and 9 in females. The right lung was involved in 14 cases, the left in 6 cases, both in 3 cases; no record in 4 cases. Pain was one of the earliest symptoms, and was felt often a day or two before the temperature rose noticeably or physical signs could be made out. Only 5 of the 27 cases were ushered in by a chill, and of these 5, 3 were fatal. The rarity of the initial chill in these cases is worthy of note, also the fact that the absence of chill did not indicate, as it usually does, a milder course of the disease.

Pneumonia after operations seems to be much more frequent in England and Germany than in this country. In the clinic at Erlangen during the period 1887 to 1894 there were 38 ether narcoses with 6 pneumonias, of which 4 were fatal. During the same period there

were 300 narcoses with chloroform with 15 pneumonias, 4 fatal. In abdominal operations the use of ether seems to be followed by pneumonia with especial frequency.

Whitney[64] suggests that the mouth should be disinfected before taking the anæsthetic, to destroy the specific germ and prevent its descending into the lung. Lucas has raised the question whether the frequent occurrence of pneumonia after operations may not sometimes be due to infection from the inhaler and suggests measures for avoiding the danger.[65] Bad ether may contribute to the result in some cases.

When we consider, however, the great frequency of pneumonia after operations before the days of anæsthetics, it is evident that their use prevents vastly more cases than it causes, if indeed it is ever the active agent in the production of the disease. It seems much more fair to say of ether and chloroform that they sometimes fail to protect the patient from post-operative pneumonia, than that they ever bring about an attack. This protection comes probably through lessening of shock and of nervous depression. It is possible also that the anæsthetic may exert a direct antagonistic influence upon the coccus.

Communicability of Pneumonia.

While pneumonia is unquestionably a communicable disease, it is not readily transmitted from person to person. From what has been already stated in regard to the very frequent presence of the specific germ in the air passages of healthy persons, it will be inferred that something more is required than simply the transfer of microbes from one individual to another in order to communicate the disease. Nevertheless, there is much in literature to show the occurrence of limited local epidemics of pneumonia, as well as the appearance of a number of cases in single households, either simultaneously or in rapid succession. In addition to this, certain houses have been observed to furnish year after year an undue proportion of cases, apparently indicating that the infecting principle lurked in the apartments.

During the building of the new Croton aqueduct in New York a large number of Italian laborers were employed. They congregated together in wretched huts along the line of the aqueduct, sleeping in a confined and contaminated atmosphere, and living in ignorance of every principle of health. Pneumonia was of very frequent occurrence among them. In 1886 Darlington[66] treated one hundred and fifty cases. The conditions were such as to invite pneumonia apart

from transmission from one person to another, yet doubtless this contributed to the result.

In Middleborough, England, there occurred in one year (1888) 367 cases of pneumonia in a population of 40,000. Halwell reports the occurrence of 50 cases in 13 days in a village of 400 inhabitants.[57]

Emmerich [58] reports an epidemic of pneumonia occurring in a prison at Amberg in 1880, and lasting for six months, in which 161 cases occurred and 46 proved fatal. In dust found beneath the flooring of the dormitory in which the cases were treated, Emmerich demonstrated the presence of the pneumococcus, and obtained results similar to Friedländer's by inoculating animals with it. Dust from the floor of other dormitories in which there had been no cases of pneumonia was examined without detecting pneumococci. After thorough cleaning and disinfection no further cases of the disease appeared.

Tyson[59] says: "Out of a ship's crew of 815, 410 have been attacked in rapid succession, and of 720 attacked 298 fell victims."

In hospitals, and under ordinary conditions in private families, there is, however, very little danger of communication. The apparent instances of such transmission are probably quite as often due to depressing causes incident to grave illness in the household, or to prolonged and exhausting attendance at the bedside. In my experience I have seen but a single instance in which I thought the disease was directly communicated, and this was in the person of a hospital nurse, who while in attendance upon a patient with pneumonia was himself fatally attacked.

As, however, it has been shown by Flügge and others that in the act of coughing a fine spray may be formed from the expectoration, which spray is capable of floating in the air for an hour or more before it subsides, it is quite possible that the inhalation of this may convey the specific germs directly into the deeper air passages and thus excite an attack. An instance of communication apparently in this way was narrated by Girdner in a discussion before the New York Academy of Medicine, December 17th, 1896. In this case the nurse, who was very constant and faithful in her duties, lifted the patient's head at each attack of coughing, and held the towel into which he expectorated. She developed fatal pneumonia during the progress of the case.

The many similar instances in literature leave little room to doubt that the disease is communicable under very favorable conditions, and it is therefore incumbent upon the medical attendant in each case to adopt precautions against such infection.

As to the etiology of pneumonia in general, we are obliged to

admit that in a large proportion of cases the attack seems to come on spontaneously, that is to say, there is no appreciable antecedent condition which appears to hold a causal relation to it.

Treatment.

The first step in the treatment of pneumonia is to place the patient in a single bed, so situated as to be accessible from either side. Space also should be left for passing between the head of the bed and the wall. The room should be large and well ventilated and if practicable should be lighted by a window on each side of the head of the bed, and not by one at the foot. The temperature should be kept at about 65° F., the attendants wearing a little extra clothing if necessary, especially for the feet. The air of the room should be completely changed every two or three hours according to the size of the apartment, and in the intervals a window should be kept slightly open, the bed being protected by a screen if required.

The modern high bedstead now generally adopted in hospitals adds greatly to the comfort of the physician and attendants. In view of the probable use of water more or less freely for sponging, etc., the mattress should be protected by rubber cloth.

The patient should be clothed in a soft flannel gown which should be made to open in front to facilitate examinations, local applications, etc. The bed clothes should be light and not so abundant as to bundle up the patient too much or to retain the exhalations from the body.

Clean cloths should be provided for receiving the expectoration, and these should be burned before they have an opportunity to dry. The sheets should be changed frequently and "antiseptic precautions" observed in every particular.

Alimentation.—Undoubtedly the usual tendency is to give too much food to pneumonic patients. The extreme adynamia sometimes seen in the course of the disease, together with the oft-repeated injunction of lecturers and writers "to keep up the strength," frequently results in as much nourishment being crowded upon the patient as he can be induced to swallow. But the febrile condition is unfavorable to digestion, and fermentation with consequent flatulence often results. The abdominal distention in turn interferes with the descent of the diaphragm and adds to the difficulty of respiration.

All this is the result of a mistaken zeal in the matter of feeding. The fact is overlooked that the loss of strength is due to the intensity of the infection which poisons nerve and muscle, and not to lack of nutriment. Furthermore, even if the food were digested and absorbed into the circulation, there would remain the equally impor-

tant function of assimilation to be accomplished before the system could profit by the nutritive material added to the blood. Assimilation depends largely upon oxidation, and when the respiration is seriously embarassed hæmatosis is correspondingly imperfect. Under these conditions an excess of pabulum, even if taken into the blood current, can only add to the burden of the system.

The condition of the alimentary canal, therefore, should be constantly watched, and only so much food and of such a quality should be given as will be completely digested and assimilated. The appearance of stomach or intestinal flatulence, or of a thick and muddy urine, should lead to a readjustment of the diet. This may consist at first chiefly of milk, of which forty ounces per diem will usually give a better result than a larger quantity. If not readily digested the milk may be peptonized, and if it acquires a bitter taste by the process being continued too long, this may be covered by the additon of a little coffee. Kumyss or matzoon may be substituted wholly or in part, if more agreeable to the patient.

Beef tea, or expressed beef juice, may be used alternately with the milk to relieve the monotony of the diet.

There are several food preparations on the market that supply both nitrogenous and starchy elements already acted upon by their appropriate digestive ferments. These preparations contain some alcohol, added to preserve them, and they therefore serve both as food and stimulant. Such products, coming from reputable laboratories, may be relied upon as to their composition, and can be made to fill an important place in supplementing other articles of diet. They are not likely to cause flatuence, and are generally acceptable to the patient.

During the pyrexia, whatever food is given should be in liquid form and in small quantities at short intervals. After the crisis, if the digestion be fairly good, the diet may be more generous; eggs, fish, and finally meat being added as the appetite returns.

Throughout the disease the patient should have as much water as he desires. An active diuresis tends to carry off the toxins in the blood, and the best diuretic is pure water in abundance.

Treatment of the Local Condition.

When we have pneumonia we have an area of lung in which every air cell represents a tiny culture tube filled with a culture medium, and harboring a colony of diplococci; the lung tissue meantime being nourished by a separate set of nutrient vessels which are not materially involved in the process. This is the essential condition; incidentally more or less breathing surface is withdrawn from use,

and the system is flooded with a toxin more or less virulent. Unhappily what is incidental in the situation is of much more serious import than what is essential.

Now it is clear that this state of things is absolutely unique. We have not, and for anatomical reasons we cannot have, anything resembling it in any other locality. Analogy, therefore, can aid but little if at all in the matter of treatment. Nor can therapeutical methods based upon former pathological conceptions be utilized otherwise than as they may furnish authenticated facts having a value apart from their theoretical setting. Hence, there would be little practical utility in entering upon the history of the treatment of pneumonia. Until very recently, except so far as it was wholly empirical, this has merely reflected the current views as to the proper management of inflammation in general. The local process having been regarded as inflammatory, the disease has shared in turn the onslaught of the lancet, of mercury, of tartar emetic, and of all the long list of antiphlogistics. Even up to the present moment we hear of the use of certain drugs or methods to "reduce the inflammation" at the same time that the infectious nature of the disease is recognized. With this recognition, however, many, if not most authorities show a disposition toward therapeutic nihilism. "The disease is infectious and self-limited, there is nothing for us to do but to guide it if possible to a favorable termination." But the generalization that would classify pneumonia with scarlet fever and smallpox simply because it is technically infectious, is almost as unfortunate as that which would label it an inflammation and give it nosological fellowship with everything that ends in *itis*.

Keeping before us the nature of the disease, it is evident that a rational treatment must have both a local and a general bearing. The local bearing will require in the first place measures tending to lessen the production of toxic material in the lung, and in the second place measures that obviate so far as may be the mechanical obstacles to respiration. The general bearing will be in the direction of minimizing the toxic effects upon the system at large, or enabling the system to bear up under these effects.

Over and above the indications thus afforded, special conditions which may arise will require to be met by special measures.

Moving upon these lines the first object is so to act upon the blood as to make the fibrin which is exuded from it into the air cells as unfit a medium as possible for the growth of the specific germ.

In considering the possibility of thus restraining the activity of the local process we come at once upon two facts important for our encouragement. The first is that the life of the diplococcus is very

short, not exceeding ten or twelve days at the most in artificial cultures. The second is that of all known germs this is perhaps the most sensitive to its environment, laboratory experience showing that it can be cultivated successfully only by the most careful attention to its habits and peculiarities. The slightest deviation from the conditions these impose puts an end to its growth. Furthermore, the probability of successfully inhibiting the action of a germ through the influence of an agent diffused in the blood is greatly enhanced if the germ is located in the lung. This is due to the fact that the whole mass of the blood passes through the comparatively small pulmonary circulation every time that it traverses the vastly greater systemic circuit. Hence any substance in the blood comes into much more intimate contact with a germ in the lung than it would with a germ placed elsewhere, and the assault is proportionately concentrated and energetic.

It is true that to be fully effective a germicide designed to act within the air cell must be employed before the circulation in the functional capillaries is arrested. After such arrest it can reach its destination only by the very narrow channel of the nutritive blood supply. But as the pressure of the exudate is the ultimate factor in closing the functional vessels (whatever coagulating influence the morbid process may have exerted) it is not until consolidation is complete that access through these vessels is entirely cut off. It is also encouraging to note, in looking back, that various methods have been found useful in a marked degree, and have even been credited with the power of cutting short the disease in a certain proportion of cases. These measures were employed either before germs were known, or certainly without any germicidal intent, but we now feel that they owed their value chiefly to their antimicrobic influence.

Mercury.—Foremost among these is the use of mercury. Half a century ago this was universal, and it is hard to believe that intelligent and acute clinicians, men, for example, who could draw such an admirable picture of pneumonia as that furnished by Sir Thomas Watson, could have been wholly deceived in their estimate of the value of this agent. Watson[60] says (the italics are mine): "Many persons I am persuaded are saved by treatment of this kind, pushed to slight ptyalism: *the effusion of lymph,* tending to spoil the texture of the lung, *is arrested, and the lymph already effused begins to be absorbed:* and the ease and comfort of the patient, *as well as the alteration for the better of the physical signs,* attest the healing qualities of the remedy."

Twenty-five years later, Dr. James R. Leaming[61] writes: "I well remember my astonishment when thirty years ago the late Dr. E. P.

Cammann ordered a large dose of calomel in an attack of intercurrent pneumonia in a case of chronic phthisis, and my gratification at seeing the disease successfully controlled thereby. It was perhaps the most practical of all the valuable lessons I received from him. . . . The admirable *sedative effect* of calomel when needed is best seen when it is placed dry upon the tongue of the patient. . . . *The temperature at once begins to fall* (italics mine), *the heart to gain strength*," etc. . . .

Personally I have witnessed too often both in Dr. Leaming's practice and my own the beneficial effect in pneumonia of a single dose of thirty to fifty grains of calomel, given early, not to share to some extent in the enthusiasm of the writer.

The New York *Medical Journal* for June and July, 1879, contains a very interesting report on the "sedative" dose of calomel, made to the Therapeutical Society of New York by Dr. Putnam Jacobi, Secretary of the Committee on Antipyretics. It is a summary of the results of a collective investigation covering fifty cases in which large doses (twenty to sixty grains) of calomel were given. In most cases the object was to reduce an inflammatory process. In nearly all there was a marked decline of temperature within twelve to twenty-four hours after the dose. Fourteen cases were of croupous pneumonia, all of them severe. Of these patients thirteen recovered and one died. This is a remarkable showing, and it is impossible to read the report and not yield to the conviction that in some of these cases the calomel turned the scale toward recovery. In no case was there excessive purging from so large a dose. Stomatitis occurred only twice in the fifty cases, and produced no serious inconvenience.

At the present time we can scarcely accord to mercury the "antiphlogistic" property with which it was formerly credited, and Leaming does not ascribe the benefit derived from it to such a quality but to its *sedative action* when given in the (large) *sedative dose*. We can understand, however, that when an agent so inimical to germ growth is taken into the blood and effused into the air cells along with the fibrin that is to act as a culture medium it must have an effect to retard at least the activity of germ formation in that medium. Laboratory experiments show that the pneumococcus is peculiarly sensitive to mercury; and with so large a quantity of calomel diffused through the alimentary canal it is easy to conceive that enough mercury, probably in the form of the bichloride, should be absorbed and exuded with the fibrin to sensibly affect the pabulum upon which the microbe feeds. *A fortiori* would this be the result when the blood is so charged with mercury as to produce the phenomena of ptyalism.

More recently, Pieragnoli[92] strongly recommended the employment

of calomel in croupous pneumonia. His method consisted in the daily administration of calomel combined with opium and in the avoidance of expectorants in the first few days of the attack. His results were very satisfactory. Of five patients to whom the calomel was not given all died, of fifteen who were treated with calomel all but one recovered. Equally good was the result in children. The course of the disease was milder, the infiltration was less firm, and the wandering of the disease in the lung less marked. The appearance of diarrhœa, also, seemed to have a favorable influence.

Smarkovsky,[63] of Moscow, claims that calomel given in doses of 5 or 6 cgm. (gr. $\frac{3}{4}$–1) every hour until a purgative effect is produced, is capable of jugulating croupous pneumonia and causing its abortion. This does not result, he observes, from any direct influence of the calomel upon the pulmonary lesion, but from a general antiseptic action upon the toxic material circulating in the blood, thus augmenting the resistance of the organism to the morbid local process.

Granting the major proposition, it would be more reasonable to infer that the drug acted toward limiting the production of the poison, rather than its destruction after it has reached the current of the blood.

For almost fifty years Clemens, of Frankfort, has been employing inhalations of *chloroform* in pneumonia with a view to its sedative action upon the nervous system and its anticoagulating (?) effect upon the blood. His success, as will be seen later, has been remarkable, and others following his example have obtained like results. Here again we have a powerful germicide which in this case is not only introduced into the blood, but is at the same time brought into direct contact with the culture medium itself, up to the time when complete consolidation excludes it from the air cells.

Later we have the introduction of *quinine* in large doses, given with a view to its antipyretic effect. Many authorities, including Flint,[47] believe that it is possible in this way to abort a pneumonia in its initial stage. Flint says: "As long ago as 1861, I was led by the results of the analysis of a considerable number of cases in which sulphate of quinine was given to the extent of only fifteen grains daily, to the conclusion that this remedy exerted a marked curative influence upon the disease. I can now (1881) bear testimony to the fact that, given in larger doses, namely twenty to thirty grains daily, this remedy, in a certain proportion of cases, renders the disease abortive, and that when this does not follow, the disease is often modified to a greater degree than by smaller doses. Now whatever efficacy belongs to these remedies proceeds evidently not from any direct effect upon the pulmonary affection, but from a controlling

influence over the pyrexia, thus sustaining the doctrine that the disease is an essential fever."

How this abortion is to be effected simply by acting upon the heat centre there is no attempt to explain.

Hare[64] expresses the belief that quinine with aconite or veratrum viride, employed before consolidation has taken place, has the power of so modifying the hyperæmia in the affected area as practically to abort the local process and prevent exudation.

He warns, however, against the assumption that every case if left untreated would necessarily go through all its stages. He says: "Personally I believe that it does not always run a full course and that those cases, such as Bristow mentions, which get well after the second day are instances where, from one reason or another, the infecting micoorganism is incapable of carrying out its ordinary processes.* Believing this, which is based upon the best of bacteriological investigation, we should be able so to modify the process by treatment as to partly abort the illness, provided we see the patient before the microorganism has accomplished its purpose and produced such pathological changes in the pulmonary tissues that resolution and absorption processes must take place."

A. H. Kerr[65] advocates warmly the use of *creosote* in large doses in the treatment of pneumonia. He says: "I do not say that creosote is a specific in pneumonia, but I do say, and with emphasis, that it is the nearest approach to one that has yet been reached." He dwells upon its being eliminated largely by the lungs, and thus being brought into direct contact with the lesion. It permeates the tissues rapidly, and the air at each expiration is loaded with it, as is evidenced by the odor of the room within twenty-four hours from the beginning of its use. He gives the details of a case seen within twenty-four hours after the chill. The pulse was 120, temperature 104.2° F., respiration 40. Dulness and fine crepitant râles over

* As regards this matter, we frequently hear it said of a person who has had a brief illness, that he was "threatened with pneumonia." Formerly I had little patience with this expression, believing that it necessarily meant more to the friends than it meant to the physician who employed it. But I have come to thinking that it describes very well an abortive invasion of germs, which after a brief struggle have been overcome by the resisting-power of the system. For myself, I believe that scattering germs stray into the air vesicles oftener than we suppose, but not finding a suitable nidus fail to effect a permanent lodgment. How frequently we meet with a stitch in the side accompanied by some fever, and on examination are not a little relieved by the absence of physical signs. At the next visit there is scarcely a trace of the attack remaining. For one such case coming under the notice of the physician there are probably many more for which advice is not sought. A proportion of such cases are, I believe, to be accounted for in the way I have suggested.

the base of the left lung. Ten minims of creosote were given every two hours, and for the first day a grain of opium every three hours. The following day (the third of the disease) the pulse remained at 120, temperature 104°, respiration 36. Twenty-four hours later (fourth day) pulse 96, temperature 102°, respiration 26. At the next visit (fifth day) pulse 80, temperature 99°, respiration normal, patient convalescent.

Under the head of "Note di Terapia" the *Clinica Moderna*[66] states that it has been demonstrated that clysters of creosote, each containing from twenty-five to forty drops, are of great value in pneumonia, and cause a subsidence of all the alarming phenomena of the disease. (References not given.)

Robinson[67] insists strongly upon the value of creosote inhalations from the very beginning of an attack of pneumonia, not only for their beneficial effect upon the patient, but as having a tendency to lessen the danger of infection to the attendants. He provides for the vaporization of pure beech-wood creosote in considerable amount along with the production of steam. The apparatus is placed near the patient's bed, but the atmosphere of the whole room is thoroughly impregnated with the combined vapors, so that they are inhaled by the attendants as well. He is firmly convinced of the utility of this practice, which has an evident foundation in reason.

The pneumococcus, as we have already seen, is extremely vulnerable, and while it may not be actually killed by any vapor that could be safely taken into the lung, yet there is no reason why its growth should not be inhibited to a considerable extent, and the amount and virulence of the toxin materially lessened. It is no sufficent objection to this proposition that the inhaled material could not reach the interior of the air cells in the hepatized area, since all goes to show that the most active conditions for general infection are supplied by the partly filled alveoli surrounding the consolidated focus. To these cells a gaseous germicide can easily penetrate.

As to the possibility of aborting pneumonia and the value of antiseptic inhalations, Robinson says:

"One of the points in regard to the course of acute croupous pneumonia which is most important is this: to determine, if possible definitely, whether or not pneumonia has a certain well-defined course terminating in crisis on a given day, which is, so to speak, unchangeable. In other words, is pneumonia capable of jugulation? Can we abort it by any one of our known medicinal means? This question has been answered differently by different authors. Osler, for example, denies that it can. Bristow seems to be of a somewhat different opinion, since he believes that 'in very mild cases all the symptoms may subside in three days, or even two days.'

"One thing is true, however, if we may attach faith to the experimental researches of Welch, and it is that the micrococcus lanceolatus, the admitted cause of croupous pneumonia, is a pathogenic organism, one of those least tenacious of life, and that its loss of virulence is frequent and apt to occur rapidly. Is there not in this important fact a very substantial reason why we should endeavor to employ antiseptic inhalations early in the treatment of pneumonia, before lung consolidation has taken place, and while we may yet legitimately hope that the antiseptic vapor may reach every portion of the affected pulmonary area?"

Salicylates.—Robert Liegel[68] contributes a remarkable paper in which he describes a treatment which has been successful in his hands in seventy-two consecutive cases of croupous pneumonia occurring in the miners at Leoben-Seegraben. The patients ranged from sixteen years of age to seventy-four and included many subjects of anthracosis. Eight had pulmonary emphysema, six cardiac disease. A large proportion were alcoholics. The drug relied upon was sodium salicylate in "large doses," not less than 8 gm. daily. This was given in solution, with aqua menthæ piperitis to cover the taste. No other medicine was employed except perhaps an expectorant containing ipecac, if the cough was tight and racking, and small doses of morphine when the pain was excessive. Ice was applied to the head when the temperature was above 39.5° C. (103° F.).

Under this treatment not only did recovery take place in every case, but the duration of the attack was diminished one-half. In no case did crisis occur. The temperature declined from the end of the first day, until at the end of three or four days it reached the normal, and convalescence was established. The expectoration lost its distinctive character and became catarrhal, the physical signs did not fully develop, or if present, speedily retrogressed. The microscopical examination of the sputa showed a constantly diminishing number of diplococci, until, at the end of the third or fourth day, they were found to have entirely disappeared.

In the earlier cases the medicine was suspended as soon as the temperature became normal, but this was found in a number of instances to be followed by relapse; observing this, the doses thereafter were continued for some two or three days longer, and no further relapse occurred.

Previous to the adoption of this treatment the management of the disease by the usual methods had been very unsatisfactory and the mortality excessive.

Liegel considers that the salicylate exerts a specific effect, such as it exhibits in rheumatic fever. He, however, assumes that it acts

upon the mucous membrane, increasing its secretion and thereby throwing off the exudate, as croupous membrane is thrown off from

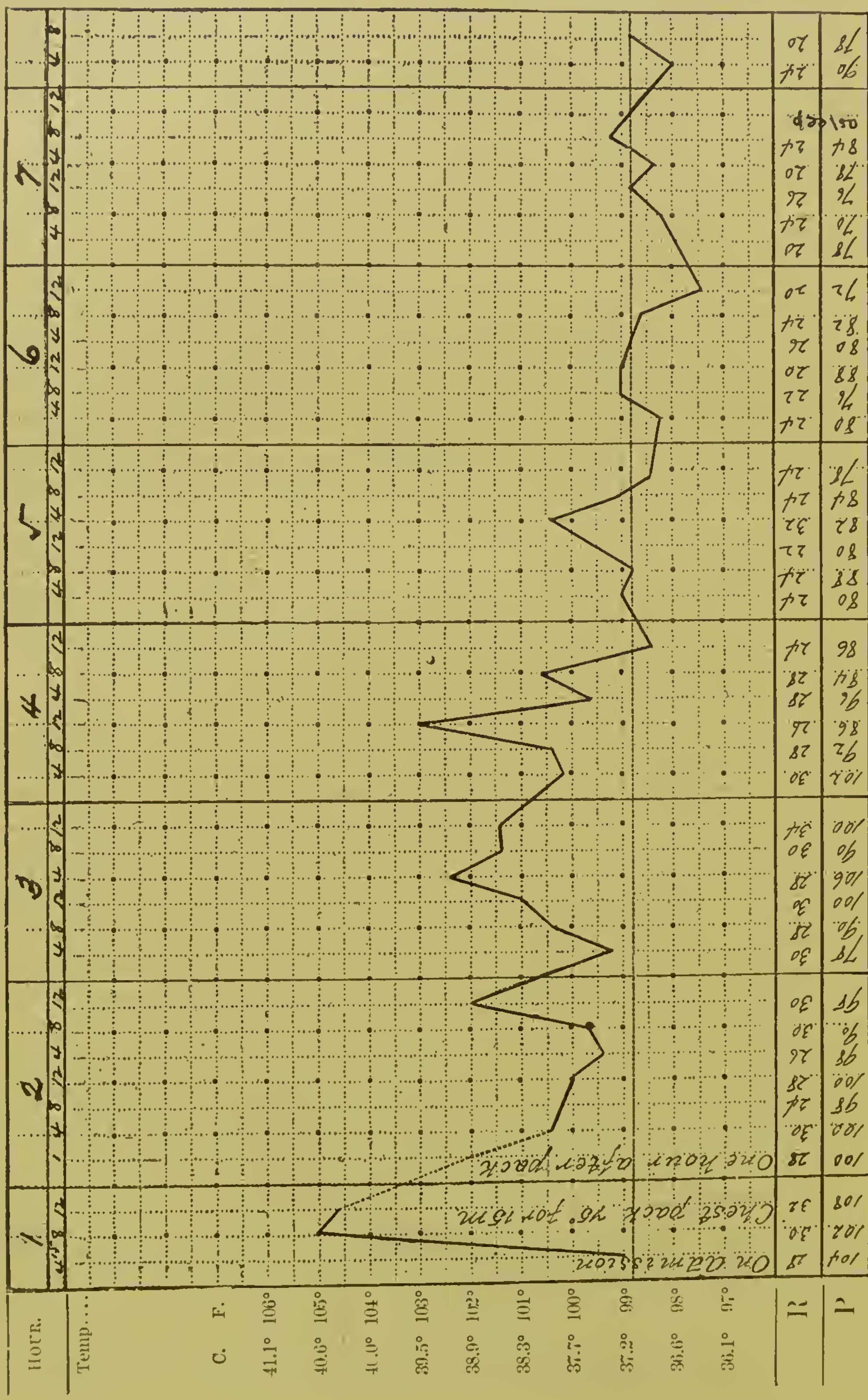

CHART No. 4.—A Case Treated with Ammonium Salicylate. Patient was admitted immediately upon the occurrence of the chill, and 20 grains of the drug were administered every four hours. Temperature reached the normal on the fourth day.

the larynx. In no instance did it give rise to any symptoms more unpleasant than a buzzing in the ears. Indeed, the dosage was fairly moderate, less than we habitually employ in the early stages of acute rheumatism, and anything like poisonous effects could scarcely be apprehended.

Liegel believes that this treatment will save nearly all cases, and he cites some instances to show that the most unfavorable conditions may be recovered from under its use. In one of these a man sixty-seven years of age was taken with pneumonia while living in a damp cellar, in which six persons were huddled together. He had been insufficiently nourished before the attack, and when first visited was found delirious and too much prostrated to be removed to the hospital. He recovered, however, in the same time as the others, notwithstanding his miserable surroundings.

This is the latest and most important illustration of the possibility of so acting upon the blood as to hinder the growth of the bacteria, and to diminish, if not prevent, the formation of toxin.

The following is from a private letter to the writer, from Dr. A. Ross Matheson, of Brooklyn. The substitution of the ammonium salicylate for the sodium salt has much to recommend it, but the latter has seemed to me to be better borne by the stomach:

"For several years I have used the salicylate of ammonium in pneumonia, more especially in those cases occurring during the grippe season and in which there was a grippe element more or less pronounced. I am now treating a case of lobar pneumonia in the third stage in which the only remedies administered have been salicylate of ammonia, codeia sulphate, and strychnia sulphate. The symptoms in this case in the beginning were formidable in the extreme, but modified early as a result, I believe, of the effects of the ammonium salicylate. I administer it in ten to fifteen grain doses, and endeavor to have the patient take from one and a half to two drachms in twenty-four hours.

"I find that ammonium salicylate has some advantages over the soda salt. It is stimulating, while the latter is more or less depressing, and it does not produce to the same extent the throat and ear disturbances. I am satisfied that it has decided value in the treatment of pneumonia."

Dr. J. H. Ferguson, of Mine La Motte, Mo., informs the writer that he has records of one hundred and six cases of pneumonia treated by him with sodium salicylate, showing one hundred recoveries and six deaths. He was led to this method by the belief that inflammation in general was intensified by uricacidæmia. He gives five grains every two hours, together with potassium citrate, to stimulate the kidneys.

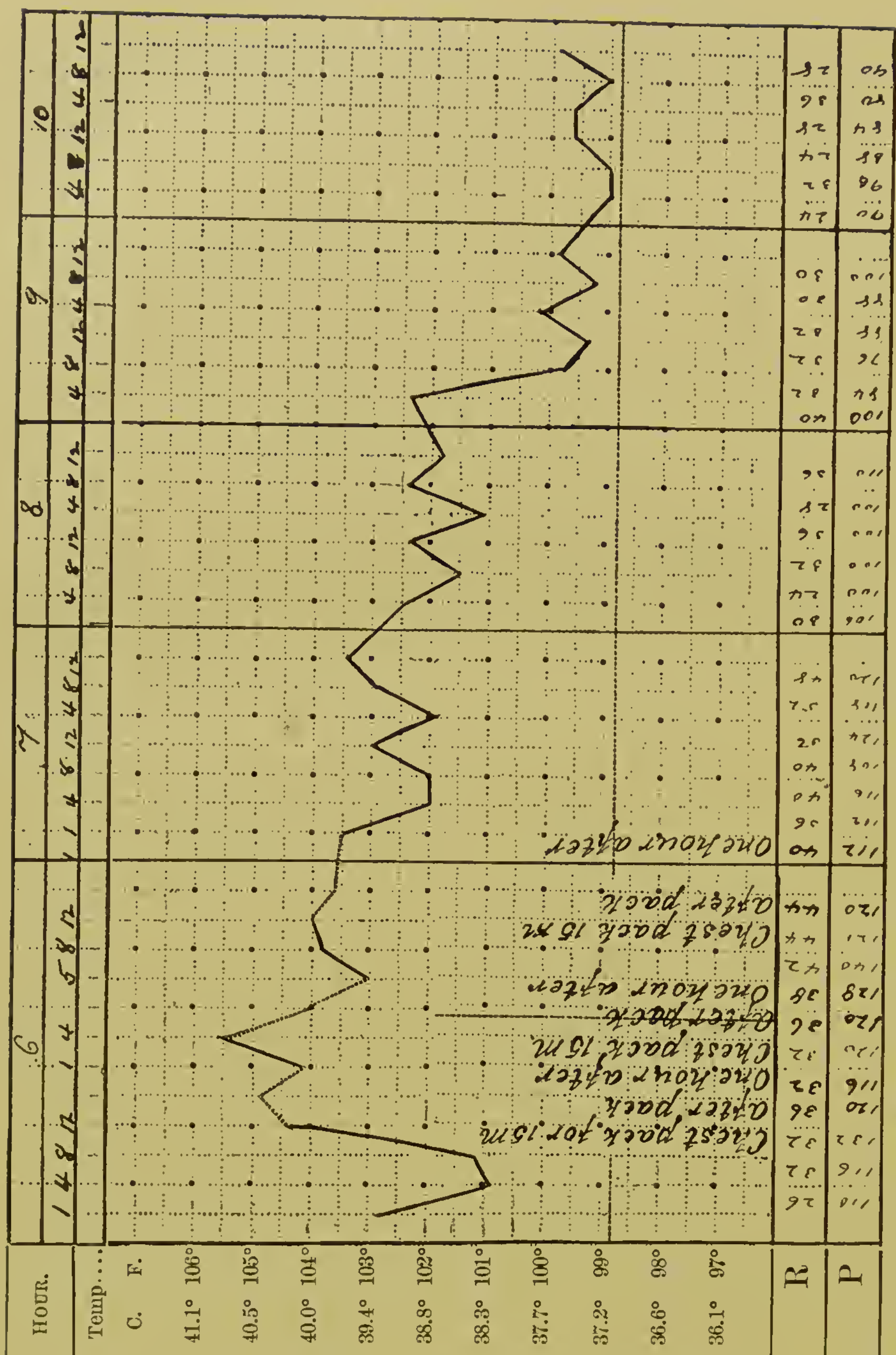

CHART No. 5.—Patient having Double Pneumonia who was Treated with Sodium Salicylate. Patient entered hospital on the third day of the disease with pneumonia of the lower right lobe. On the sixth day the left lower lobe become involved. Cold packs applied to chest for temperature above 103.5°, and 20 grains of sodium salicylate administered every four hours. Defervescence by lysis. Normal temperature on tenth day.

Salicylic acid has been employed as an antipyretic in pneumonia by different clinicians, but has not been found to possess special advantages over other remedies of that class. It has not, I believe, been used in this disease with a view to its antimicrobic effect.*

* According to Buchholz 0.15 per cent. of salicylic acid will prevent the development of bacteria in ordinary organic mixtures, and the influence of 0.005 per cent. (1 : 20,000) is plainly visible. Sodium salicylate has about the same power.—Wood's "Therapeutics, its Principles and Practice," 10th ed., Philadelphia, 1898, p. 705.

From the foregoing facts and opinions, as well as from the theoretical considerations already brought forward, it seems clear that there is ample justification for a treatment of pneumonia based largely upon the causal indication. In other words, we may reasonably expect benefit in a considerable proportion of cases from the use of means addressed directly to the germ present in the lungs. The practical question to be solved is what agent will act most powerfully upon the specific organism with least inconvenience or danger to the patient. This opens a wide field for study and observation upon which I firmly believe it is the duty of the profession to enter.

Thus far the most efficient and least harmful drug appears to be the salicylate of sodium, as employed by Liegel. As we have seen, seventy-two consecutive cases, many of them most unpromising, have been treated with it without a death. This is a very remarkable record, and certainly recommends the treatment most strongly for further trial. Apart from the experience of Liegel, it does not appear unlikely that a drug which is capable of producing such decided results in acute rheumatism should be effective against an organism so sensitive as the pneumococcus.

Liegel did not observe any depressing effect from the salicylate in the doses he employed (8 gm. daily), but such if apprehended could be guarded against by the use of strychnine, etc.

Creosote has been found useful by several observers and deserves further trial. It may be given by the mouth or the rectum, or employed by inhalation. The dose by the mouth is ten to fifteen minims every two or three hours, largely diluted; by the rectum twenty-five to forty minims in a clyster. By inhalation it is useful only as an adjunct.

The following case, in which creosote was employed, was seen by the writer in consultation with Dr. Bainbridge, of this city, January 9th, 1899.

Miss C——, aged 46, had suffered from influenza in November, 1898, and from a second attack beginning January 1st, 1899. She was first seen by Dr. B. January 6th, when signs of pneumonia were present in the right base. On the seventh, there was complete consolidation at the right base with beginning signs in front over the right lower and middle lobes. Pain in bones, relieved by a few doses of phenacetin and salophen.

On the 8th, nitroglycerin and sparteine sulphate were begun. Alcohol, which seemed to be indicated, caused marked cerebral excitement. The right middle and lower lobes were solid.

On the 9th, the temperature reached 105° F. and the writer was called in consultation. The treatment agreed upon included strychnine sulphate by the mouth, and creosote, 20 minims, with sodium bromide, 25 gr., by the rectum. This was repeated every four hours,

the creosote and bromide being mixed with the white of an egg to which three teaspoonfuls of brandy were added.

On the 10th, a small area of beginning consolidation appeared at the angle of the left scapula, and a few râles were heard in the left axilla. The enemata causing discomfort, the bromide was reduced to 20 gr. and the creosote to 10 minims.

On the 11th, there were signs of pleurisy in the left axilla. Later, a brief attack of pulmonary œdema occurred, and the pulse rose to

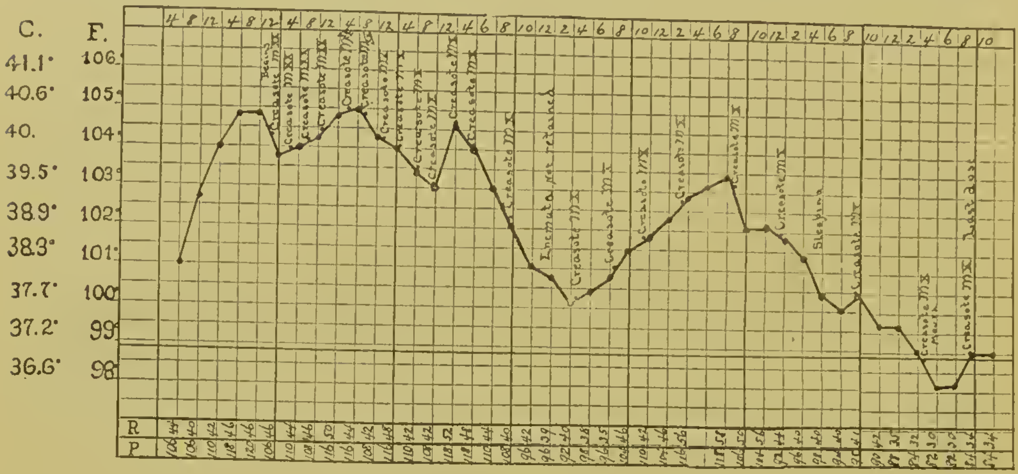

CHART No. 6.

130 and the respiration to 60. The attack yielded to brisk counter-irritation and inhalations of oxygen. During the night of 12th–13th, the patient was greatly depressed and the heart was very weak. Stimulants increased.

On the 14th, the patient was very comfortable; convalescent.

In this case there was pseudo-crisis on the sixth day, with subsequent rise of temperature and defervescence by lysis, the temperature reaching the normal on the eighth day (see chart No. 6).

Carbolic acid may perhaps be found to have some advantages over creosote. It is less disagreeable to take, and probably less irritating to the stomach. It is readily taken into the system, as is shown by its speedy appearance in the urine. The usual dosage may be greatly exceeded with perfect safety. Wigglesworth[69] gives as much as six grains every two hours day and night in the treatment of scarlatina, continuing it until the risk of infection disappears. Dr. Jackson, of Alnwick, Eng., in a letter to the writer, says that he gave to a patient suffering from charbon three drachms in the first twenty-four hours, two drachms in the second, and one and one-half drachms during each day thereafter till the end of the fortnight. It was retained when everything else was vomited, and no ill effect was experienced except a moderate albuminuria* which disappeared

* This may have been the result of the infection, and not of the acid.

in a few weeks. The patient was rescued from an apparently hopeless condition.

I have myself given one hundred and thirty to one hundred and fifty minims of the liquefied acid in twenty-four hours, for several days, without the least unpleasant result. The urine had a slightly greenish color when voided, and became perfectly black after standing a few days, but contained no albumin. Declat cured intermittent fever with carbolic acid when quinine had failed, and if it is capable of destroying the plasmodium in the blood it would doubtless be capable of inhibiting the growth of the pneumonia germs in the alveolar contents.

Corrosive sublimate is believed by many to act favorably in diphtheria when taken in quantity sufficient to act upon the whole mass of the blood, but yet within the limits of safety. We have already seen that there is evidence that calomel in a large dose may be very useful in pneumonia, and it is quite possible that still better effects might be obtained from the more soluble salt. Skoda employed it, sixty years ago, in pneumonia, with a mortality of 14.5 per cent.[2]

Almost immediately upon the discovery of the anæsthetic property of *chloroform*, Clemens,[70] of Frankfort-on-the-Main, employed it to relieve the pain and shortness of breath belonging to the early stages of pneumonia. His success with it was great, and he was still employing it at the date of his last communication in 1889. He claims that he has given it in every case of pneumonia occurring in his private practice since about 1850, and with such success that he has not lost a single patient. He attributes this to the soothing effect upon the nervous system, the lessening of shock, and the freer respiration resulting from the absence of pain. But he states that in addition to these effects there is often a marked hastening of the crisis, and that the average duration of the disease is lessened. His explanation is that the chloroform defibrinates the blood in the lungs and prevents hepatization.

Baumgartner was one of the first to make extensive trials with inhalations of ether and chloroform in pneumonia, and found that in this as in other chest diseases the feeling of constriction, the stitch, the expectoration, and the sleeplessness were relieved. At the same time the abundant secretion from the bronchial membrane which, especially in the case of ether inhalation, marked the beginning of the treatment subsided as the treatment progressed. Wucherer published a pamphlet on the subject as early as 1848, and Varrentrapp and Thiele treated a great number of cases of pneumonia with inhalations of chloroform.

Oertel[71] found decided benefit from inhalations of chloroform,

and refers to the experience of Baumgartner, Wucherer, and Varrentrapp, Thiele, and others which agree as to the relief which may be afforded by their use. Oertel employed them largely in Pfeiffer's clinic in Munich, from 1860–1863, mostly in the advanced stages of the disease, about the fifth or sixth day, in cases in which there were extensive hepatization and marked involvement of the pleura, rendering the breathing irregular, frequent, and superficial; when the expectoration was more or less suppressed, and the viscid exudate obstructed the air tubes; when coarse râles were heard over large areas, and when rapidly increasing cyanosis indicated insufficient aeration of the blood. Frequently the inhalations were repeated as often as five or six times in twenty-four hours and pushed to commencing narcosis. The results were most satisfactory. The respiration became deeper; the pleuritic pain was relieved, the cough was lessened, and the sense of oppression in the chest disappeared. These results were maintained for a longer or shorter period after each inhalation, and were not entirely lost during the intervals. The râles were diminished; a more or less free expectoration was established; cyanosis was less marked; and for the most part the treatment was successful in bridging over the critical period. Oertel sums up his experience as follows: "I consider the inhalation of chloroform when the above indications are present as a means of treatment in pneumonia that would be difficult to replace by any other."

As a contraindication he regards disposition to headache, vertigo with confusion, decided congestion of both lungs, and finally general depression. He insists that if the inhalations of chloroform are to be of real value in the treatment of pneumonia, they must be administered by the physician himself.

Now in view of the hastening of the crisis and the shortening of the attack observed by Clemens, and the general improvement of the patient's condition so strongly insisted on by Oertel, it may fairly be asked whether these inhalations of chloroform do not have a direct effect upon the exudate to render it an unfit medium for the culture of the pneumococcus. Experiments conducted by Dr. J. S. Thacher, Pathologist at the Presbyterian Hospital, New York, at the suggestion of the writer, showed that this organism was very sensitive to chloroform. The penetration of chloroform vapor to all parts of the lung is attested by the familiar facts of anæsthesia. Nor is it impossible that the whole mass of the blood should become so impregnated with the agent as to render the exudate from it an unfriendly medium for the growth of the coccus. We know how in the case of anæsthesia by ether the whole body, solids as well as fluids, becomes permeated by the odor, and how long a time elapses before it ceases to

be apparent in the breath. Everything leads us to suppose that the diffusion of chloroform through the system is equally complete, though its odor being less powerful, we have not the same evidence of its presence.

For the purpose in view it would by no means be necessary that the life of the organism should be destroyed, but only that its multiplication should be prevented, something which is very much more easily accomplished.

I have found that chloroform may advantageously be given in connection with oxygen by adding one or two drachms to the water in the wash-bottle. Though the chloroform settles at once to the bottom of the bottle, the agitation caused by the bubbling of the gas through the water insures the vaporization of enough to produce a considerable narcotic effect. Aside from any action upon the germs, the chloroform allays pain, soothes nervous agitation, and promotes sleep. This method of administration will be sufficient when only a moderate effect is desired, but if the abortive action of chloroform is aimed at, a more concentrated vapor will need to be inhaled.

Other substances besides chloroform have been proposed as inhalants. *Carbolic acid* from its volatility as well as its germicidal property would suggest itself at once. So far from being an irritant, it is, when properly diluted, a local anodyne, and its vapor can be taken into the lungs in considerable strength without causing inconvenience. In some experiments I have made carbolic acid was used with chloroform, and apparently with good effect.

The effect of *quinine* in large doses has been already considered. It has been given for its antipyretic effect and as a tonic to increase the vital resistance. Much more powerful antipyretics and equally good tonics, however, have failed to exhibit the same beneficial action in pneumonia. But we know how quinine enters into the blood and destroys the malarial organism, and with this demonstration of its germicidal power we can well understand that other germs as well as the plasmodium may succumb to it. If given with a view to abort the attack the daily dose should be not less than 30 to 40 gr. If the resulting cinchonism is severe, it can be relieved by full doses of one of the bromides, preferably, in this case, the bromide of ammonium.

The attempt to cut short an attack of pneumonia will be more likely to be successful the earlier it is begun. If it is determined to adopt this line of treatment it would be well to begin with the administration of 20 to 30 gr. of calomel.* This will at least insure a thor-

* The calomel should be placed dry on the tongue and washed down with as little

ough cleansing of the alimentary canal, and probably will also increase the secretion from the liver and facilitate the portal circulation. These will be points of vantage gained, and if, as will be likely to be the case, it is followed by a considerable fall of temperature, it will open the way to the use of other germicides. The choice among these will be decided by the preference of the individual practitioner. It need not necessarily be limited to a single agent. Thus sodium salicylate, which has more or less of a depressing tendency, may be given by the mouth, while at the same time the patient is receiving enemata of creosote, which in medicinal quantities is a stimulant. Or, while a germicide is taken by mouth or rectum, chloroform may be given by inhalation. This will be specially indicated in cases in which the pain is very severe or insomnia is present.

While treatment of this kind is most likely to be effective if early resorted to, yet it should be attempted at any time during the pyrexia. For we can never appreciate how much of microbic activity may be going on outside of the hepatized area, either without physical signs or with only the signs indicating congestion.

It is not to be expected that an obvious result will be obtained within a few hours. In Liegel's cases the temperature remained unchanged until the end of the first day, and when abortion has followed the use of other methods the same delay has usually been observed. Even if it were possible to immediately cut short the production of toxin, some time would be required for the elimination of that already in the blood, and meantime the fever would continue.

Next to attempts to inhibit directly the growth of the bacterium and the formation of toxin, the local indication is to obviate as far as possible the effects of the obstruction of respiration and circulation. These two forms of obstruction are so closely allied in their results that for our present purpose they may properly be considered as one. They play a very important part in the history of pneumonia, causing directly or indirectly a greater share of the mortality than is caused by the toxins circulating in the blood.

Bloodletting.—In no disease was the lancet employed during the first half of the present century more freely and more indiscriminately than in pneumonia. The theory then in vogue as to the nature of the disease made this treatment seem natural, and it must be admitted that in the majority of cases many of the symptoms were alleviated for a time after a copious bleeding. When this was resorted to early, the pain was relieved, the breathing became freer and less frequent, and

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water as possible. By withholding fluids for about three hours the danger of excessive purging will be avoided.

the pulse lost the hard, tense character supposed to be so typical of inflammation. The temperature in those days was not noted. Then, too, the thickness of the "buffy coat" and the "cupping" of the clot were pointed to as showing how urgent had been the necessity for letting blood. Balfour[72] gives a very vivid picture of this treatment in his presidential address before the British Medical Association, session of 1898.

It cannot be said, however, that the testimony even of the writers of that day was very favorable to the practice. Thus it is recorded that in Berne, in 1762, ninety-five cases of pneumonia were treated by bleeding with eighty-five deaths, while of seventy-seven treated without bleeding only ten were fatal. But these bleedings were practised for the most part early in the attack, and before the pulmonary obstruction became a prominent factor in the case. As a means of relieving this latter condition the practice is once more gaining in favor.

Osler[23] says: "To bleed at the very onset in robust, healthy individuals in whom the disease sets in with great intensity and high fever is, I believe, a good practice. I have seen instances in which it was very beneficial in relieving the pain and the dyspnœa, reducing the temperature and allaying the cerebral symptoms."

And although the lancet has so far passed out of use that many a practitioner of the present day would scarcely know how to open a vein, it is by no means certain that a good many lives might not be saved by such a timely and judicious bloodletting as would relieve the overdistended venous system and give a measure of ease to the laboring right ventricle. Many recent writers favor the practice under certain conditions. Osler took from 25 to 30 oz. of blood in cases which he thought it indicated, but adds that he had seen only one of twelve or fifteen cases so treated that recovered. Maragnioni Felice and Cantani resort to it sometimes for its hydraulic effects. Bianchi favors it, especially in children, when great dilatation of the right auricle is present. Liebermeister upholds it when œdema occurs in the unaffected lung. Fowler[73] says:

"Cyanosis and signs of overdistention of the right side of the heart with epigastric pulsation and prominence of the jugular veins and a small and irregular pulse, are indications for venesection, and relief is generally given when 6 to 8 oz. of blood have been withdrawn. The improvement is perhaps most obvious in cases accompanied by or following bronchitis, but unfortunately it is as a rule of only short duration."

Were it not that much the same result may be brought about with less drain upon the system, as we shall see hereafter, the indication

would, no doubt, often be present for the abstraction of blood, and as it is, whenever it becomes evident that the right heart is unduly distended and is beginning to flag in its efforts to force so large a mass of blood through the obstructed pulmonary capillaries, and when adequate relief is not obtained by diverting a greater proportion of the blood into the arteries, it is the duty of the physician to open a vein and allow blood to flow until the venous tension is relieved. In children, however, the indication may be better met by the use of a number of leeches proportioned to the age and strength of the patient. Still, bloodletting is, at the best, a measure to be adopted only in extreme cases, and, like any remedy so employed, cannot be expected to produce brilliant numerical results. But, if it saves only a few otherwise hopeless cases its use is amply justified.

Nitrites.—Except in some extreme cases, however, most of the good and none of the bad effects of bleeding may be obtained by withdrawing blood from the veins and storing it up in the arteries. This is effected by the use of that class of medicines which have the power of relaxing the arterial system. Chief among these are the nitrites, but the property is shared in a less degree by numerous other remedies, notably by aconite, the value of which in inflammatory diseases accompanied by high arterial tension is now universally admitted. It was in connection with this drug that the idea of "bleeding a patient into his own vessels" was first suggested, and the phrase well expresses the peculiar action of this class of medicines. By their specific effect upon the vasomotor nerves they cause a relaxation of the muscular coat and a consequent dilatation of the whole arterial system. The change in capacity which may be effected in this manner is much greater than is generally believed. On this point Ringer says: "It has been shown that the vascular system is always in a state of semicontraction, and that by paralyzing the vasomotor nerves it is possible to double its capacity." An effect much short of this would be sufficient to produce a vast difference in the dynamics of the circulation, and to afford a large measure of relief to the overdistended venous system.

It is in this way, I contend, that we should direct our efforts in cases involving pulmonary obstruction. I am aware that there is an opinion prevalent that these drugs are contraindicated when there is feebleness of the heart's action; and there are many practitioners who would regard with a feeling akin to horror the administration of nitroglycerin, for example, when the pulse is notably small and frequent. If the condition broadly but vaguely described as heart failure were thought to be impending, the administration of such a drug would be looked upon by them as a sort of *coup de grace*. And

so it might prove to be if the feebleness of the pulse were due simply to general adynamia. But the case is altogether different when it is a mechanical rather than a vital condition we have to deal with. By increasing the capacity of the arteries we relieve the veins by exactly the amount of this increase. Lessening the pressure in the veins lessens *pari passu* the pressure in the pulmonary circulation, and with it the tumefaction of the mucous membrane and the tendency to exudation into the air passages. Relief to the respiration and lightening of the labor of the right heart are the immediate consequence.

The most prompt in its action among the nitrites is that of amyl, but its influence is so brief that it is unsuited except for extreme emergencies. Nitroglycerin acts also with great promptness, especially when given under the skin, and its effect is maintained for forty-five to sixty minutes. In doses of gr. $\frac{1}{50}$ up to $\frac{1}{10}$ it may be given without hesitation, and repeated every half-hour if required. Its effect when cyanosis is present, and the chest is filled with râles, is often most satisfactory. The lividity clears up, the râles diminish, the respiration becomes deeper and less frequent, and the pulse larger and slower. At the same time the sensorium recovers from its oppression. These results may be obtained to some degree in a period of not more than ten minutes. The dose may require to be repeated several times at intervals of fifteen to thirty minutes.

With the remedy thus administered all the advantages of blood-letting may be secured and without the loss of vitality that bleeding necessarily entails. When the conditions calling for this form of relief are more permanent it is well to employ a more lasting influence, such as is afforded by sodium nitrite. This salt is slower, but at the same time more persistent, in its action; and by doses of one or two grains every two hours the vessels may be maintained in a relaxed condition which can be added to at any time by supplementary doses of nitroglycerin should occasion require. I think it is difficult to exaggerate the value of this method when the right heart is in danger of breaking down under the strain imposed upon it. I have repeatedly seen patients rescued by it when death seemed immediately impending.

As to the dosage of nitroglycerin, the drug may be given much more freely than it usually is, provided the patient has been found, by testing with small doses, not to possess an undue susceptibility to its effect. On this point Armstrong[74] has contributed a valuable article. He cites a case mentioned by H. C. Wood, in which gr. $\frac{1}{100}$ produced insensibility, and another case in which gr. $\frac{2}{50}$ caused complete unconsciouness and loss of the radial pulse. Such cases are

due to idiosyncrasy of the patient, and not to the legitimate action of the drug. On the other hand, he mentions instances in which enormous quantities, even to 76 grains in twenty-four hours, were taken with only beneficial results. Nitroglycerin is a remedy of which tolerance is rapidly established; and Armstrong is no doubt right in his suggestion that tolerance is increased by a previous condition of vascular tension.

Practically, in pneumonia, the dose must be graduated in each case by the results obtained. So long as there is evidence on the one hand of venous repletion, and on the other of relief of this condition by the use of the drug, we are safe in pushing it without much regard to the amount given. If under its use the color of the face and lips improves and the respirations become less frequent, the indication is to continue it in the doses necessary to maintain this effect. These will seldom exceed gr. $\frac{1}{25}$ every hour, though in extreme cases this quantity or even more may be repeated every half-hour, or even oftener.

Oxygen.—Inhalations of oxygen are now very commonly resorted to in chest affections when the dyspnœa becomes severe. The use of this agent was introduced into this country by the writer in 1860. By experiments on animals he had demonstrated that by enriching the atmosphere with additional oxygen, life could be maintained for long periods under conditions of tracheal obstruction that would be immediately fatal in common air.

The introduction of compressed oxygen in cylinders for commercial purposes facilitated the use of the gas in sufficiently liberal quantities to test its real value as a therapeutic agent, and for the last twenty-five years it has occupied a prominent place in the treatment of respiratory affections and especially of pneumonia.

Its value in this disease rests on a broader foundation than is immediately apparent. It is not alone that it tends to avert suffocation. Indeed, it is very seldom that a patient with pneumonia dies directly from deprivation of oxygen. As a rule, before death from actual suffocation takes place, the heart, and particularly the right heart, gives out; and the fatal result is from asystole. This exhaustion of the right heart is a gradual process, and is brought about by the increased muscular effort required to propel the blood through the affected lung. The pulmonary ischæmia is made up of two factors, one of which is the obstruction of the vessels, and the other and very important one is the sluggishness with which blood not duly aerated circulates even through unobstructed capillaries.

It is in the relief of this latter condition that oxygen is most valuable. The moment the arterialization of the blood is improved the

circulation becomes easier and the labor of the right heart is lightened. It is a serious error, however, to defer the use of oxygen until the dyspnœa has become urgent. By its timely employment the cardiac force can be conserved and congestion of the unaffected lung territory is in a great measure prevented. But inasmuch as blood, even under the most favorable conditions, will not take up an excess of oxygen, if we delay too long and suffer the access of air to become too much restricted, no addition of oxygen acting upon the limited quantity of blood circulating in the unaffected area will suffice to restore the balance and regain the ground which has been lost.

While the results obtained from oxygen in the croupous form of pneumonia may not be so favorable as in the bronchial, still it is capable of rendering valuable aid in a large proportion of cases. A common source of disappointment lies in reserving its use until a period when, for reasons already considered, its value is comparatively limited. Even in these cases it may serve to bridge over a time of special danger, but the best results are obtained when it is given more or less freely from the moment that it becomes clear that the case is one of more than moderate severity. Its good effects will be shown in lessened frequency of the pulse and respiration, a better color of the face and lips, and fewer moist râles in the chest.

In using the compressed gas it is allowed to escape from the cylinder through a wash-bottle, the valve being so adjusted that the gas bubbles gently through the water. From the wash-bottle the gas is carried to the patient's mouth through a flexible tube provided with a mouth-piece of glass or hard rubber. If the patient is in a condition to hold this in his mouth, no more will be required. Otherwise it must be held by an attendant in such a position that the escaping gas will be drawn into the lungs with the current of inspired air.

If the patient is comatose a small flexible catheter may be passed through one nostril into the nasopharynx, and connected with the wash-bottle. In this way very little of the gas is wasted.

If it is desired to add any volatile substance to the gas inhaled, a solution containing it may be made to replace the water in the wash-bottle. Chloroform may be employed in this way.

There is no advantage in a lavish use of the gas, as the blood will take up only a very limited amount. If it escapes too freely, it adds to the sensation of breathlessness, as is the case when one faces a strong wind.

Only pure oxygen should be employed. The addition of nitrous oxide with the idea that it is more soluble in the blood should be condemned, as the oxide is useless for the purpose of respiration and interferes with the proper interchange of gases in the lungs.

In pneumonia the indication for a resort to oxygen is present as soon as the respirations exceed thirty-five per minute, and earlier than this if mucous râles develop outside of the area of consolidation, or if the lips assume a dusky hue. Under these conditions it may be given continuously, or during a prescribed number of minutes in each hour.

Treatment of the General Condition.

To combat the toxæmia we have as yet no direct means, unless it be in serum therapy, the value of which is still *sub judice*. We may hope to lessen the production of toxin by means which we have already considered, but for relief from the effects of what, in spite of our efforts, finds its way into the circulation, we must still rely upon the emunctories. The chief of these are the skin, the kidneys, and the intestinal glands. The activity of these is best promoted by the liberal use of simple cold water. This should be given as freely as the patient will take it, or if he be delirious or unconscious it should be administered at intervals in the same manner as his food.

Cathartics.—Additional stimulation of the intestinal glands may be advisable, employing cathartics selected especially with that view, and particularly calomel if it has not already been given for its abortive action. It is desirable that the bowels should be kept as free as may be without too great a drain upon the general strength, not only as promoting elimination, but as guarding against abdominal fulness and the consequent hindrance to respiration.

Diuretics.—The kidneys often fail to excrete the normal amount, indeed the urine is generally scanty, and though of high specific gravity contains much less than the normal amount of solids. Thus the most important channel of elimination is choked and its efficiency greatly impaired precisely at the time when a depurative action is most needed.

The importance of stimulating the kidneys during the pyrexia of pneumonia has not been recognized as fully as it should be. Whether with this object in view or not is not stated, but Nilsson[75] treated fifty-eight cases of pneumonia with potassium iodide, and with only three deaths. His death rate with other methods had ranged in different years from twice to three times as great. He gave 1 gm. (15 gr.) every three hours day and night; on an average each patient consumed from 40 to 50 gm.

Potassium iodide in these doses is a most efficient diuretic and it does not irritate the kidneys, as is shown by the enormous doses given with impunity in syphilitic disease. It is therefore well adapted

for use in pneumonia when a diuretic is indicated. It can very well be given by the rectum, thus saving the stomach for other uses.

Spirit of nitrous ether is also an available diuretic, and acts at the same time as a diaphoretic, a vasodilator, and a general stimulant. This combination of properties fits it admirably for use in the stage of pyrexia when the skin is dry, the urine scanty, and the pulse small and weak. It may be given in teaspoonful doses largely diluted with water, and repeated at short intervals.

Diaphoretics.—If the skin remains hot and dry notwithstanding these measures, the wet sheet applied with a blanket over it in the manner recommended by Baruch should be resorted to. This seldom fails to excite perspiration, accompanied by some degree of reduction of temperature and a marked relief of the nervous and cerebral symptoms. But the cold bath as applied in typhoid fever, with the subsequent exposure of the patient to the temperature of the room with only a sheet to cover his otherwise naked body, is a measure not to be recommended. A recession of the blood from the surface to the already congested interior can scarcely fail to be the result, and I have found the feet and legs cold under these conditions when the rectal temperature was in the neighborhood of 105° F.

The diaphoretic action of the wet sheet may be aided by the administration of Dover's powder. Pilocarpine has been recommended, but the danger that it may induce pulmonary œdema has prevented its being tested to any considerable extent.

Aside from special modes of treatment, which will be considered hereafter, the general principles to be kept in view are to sustain the heart, facilitate respiration, and husband the nerve force.

Cardiac Stmulants.—The tendency to death in pneumonia is in the direction of cardiac failure. This failure is due partly to direct toxic action upon the cardiac nerves and the heart muscle. Exhaustion as a cause of heart failure is limited principally to the right ventricle. The increased effort required to propel the blood through the obstructed pulmonary vessels continued through several days necessarily fatigues the muscular fibre, and this fatigue often goes on to the extent of paralyzing the ventricle and causing asystole.

The action of the pneumotoxin in inducing heart failure extends to the left heart as well as the right, but its effect upon the former is less disastrous as the labor required of the muscle is less severe; in fact, it may be abnormally light, owing to a diminished supply of blood received from the lungs. This is the case whenever pulmonary obstruction is a marked feature and dyspnœa a prominent symptom. When the toxic influence is pronounced, there may be a paresis of the vasomotor system, as claimed by Romberg.[76] His ex-

periments on animals lead him to believe that the circulatory embarrassment in such cases is due not so much to primary impairment of the heart's power as to vasomotor relaxation with secondary cardiac failure when the blood pressure falls below a certain point.

Van Santvoord,[77] in a series of cases of pneumonia observed in the winter of 1897–98, was able to verify the fact of this low pressure in strongly toxic cases, by means of sphygmographic tracings. He therefore claims that the first indication, viz., to sustain the action of the heart, is best met by the use of such medicines as increase arterial tension. Foremost among these he would place digitalis.

But granting the low tension, the writer believes, for reasons already given, that the condition is a conservative one, and that the welfare of the patient, so far from being promoted by a general narrowing of the arteries, would be distinctly jeopardized thereby. If the object in view were solely or principally the increase of arterial tension ergot would be the better agent.*

As a heart stimulant in these cases strychnine takes the foremost rank. Its use in small doses may be begun quite early with advantage. At first not more than gr. $\frac{1}{60}$ may be required, to be repeated every four hours. Later, $\frac{1}{50}$, $\frac{1}{40}$, $\frac{1}{30}$, and even $\frac{1}{20}$ may be advantageously employed. If necessary the remedy may be pushed to the point of producing muscular twitching. Short of this point the degree to which the nervous system is under the influence of the drug may be roughly estimated by noting to what extent the knee-jerk is increased.

When extreme cardiac stimulation becomes necessary and strychnine cannot be further pushed, Horatio Wood recommends to alternate it with cocaine.

A good article of tincture of strophanthus will give all the desirable effects of digitalis without its action upon the vasomotors. Its power is expended upon the heart muscle and not upon the vessels.

* As to any aid to the heart to come from increase of arterial tension it is difficult to see by what mechanism this aid is to be attained so long as the venous blood is dammed up in the lungs. Doubtless increasing the power of the circular fibres, or what is the same thing, diminishing the calibre of the arteries, will enable the left ventricle to transmit the force of its contractions more directly to the capillaries and through them to the venous system. But what is the advantage of this when it serves only to distend the veins more completely and adds nothing to the power that moves the venous current? For we know that *all* the blood in the body can be accommodated in the venous system alone, and is so accommodated from the moment the heart ceases to beat. Since, then, the simple retractility of the elastic coat, without any muscular aid, is sufficient to empty completely the whole arterial system, why force the muscular coat to aid in doing what is already only too effectively accomplished?

It is much quicker in its action than digitalis, its effect upon the pulse rate being noticeable within an hour. Fraser[78] considers its action upon the heart to be many times greater than that of digitalis. It possesses a very decided diuretic power, which is of no small value when the urine is scanty and the kidneys are not active in carrying off the toxin accumulated in the blood.

Tincture of strophanthus may be given in doses of four to eight drops, hypodermatically if necessary. Indeed, in all urgent cases, the cardiac stimulants capable of being administered in this way should be so employed.

Delafield, in his lectures at the College of Physicians and Surgeons, New York, asserts his belief that convallaria exerts a relatively greater action upon the *right* side of the heart, and he therefore recommends its use when the pulmonary circulation is obstructed.

Other cardiac remedies are caffeine, sparteine, adonidine, theobromine, etc. Caffeine is capable of rendering good service, the others are seldom employed. A clyster of half a pint of hot strong coffee, strongly recommended by Beverley Robinson, I have often found extremely useful. From the first the use of coffee as a beverage is to be encouraged unless contraindicated by sleeplessness.

Belladonna is of special value at the crisis to combat the tendency to collapse with cold perspiration that seems to be brought about by withdrawal of the stimulus of fever. It is indicated whenever the hands are cold and moist, the pulse is small, the senses are dulled, the brain is torpid. It is best administred as atropine, and hypodermatically.

Alcohol.—In all cases with an asthenic tendency alcohol should be resorted to in good season. The dose at first may be small, perhaps only two or three drachms of brandy or whiskey or an equivalent amount of wine, every two or three hours. But if the pulse grows smaller, and its frequency rises out of proportion to the temperature, the quantity should be increased so long as by so doing these symptoms are held in check. Particularly in subjects habituated to the use of alcohol a liberal use of this stimulant will be required. There can be no greater mistake than to put a patient suffering from pneumonia upon half an ounce of whiskey every two or three hours when he is accustomed in health to consume the better part of a pint every day of his life. The very frequent supervention of delirium tremens in the course of pneumonia is probably due to the shock of infection acting upon the brain cells already enfeebled by the chronic effect of alcohol. It is not safe to attempt its management under these circumstances by withdrawing the stimulant, as is usually done in uncomplicated cases. Enough alcohol must be given to avert the collapse

which will ensue if to the depressing effect of the toxæmia a marked reduction of the accustomed stimulation is added. Each case must be studied by itself. Tremor, wakefulness that cannot be overcome by a reasonable use of hypnotics, a dry tongue, a rapid, feeble pulse, coarse râles in areas not invaded by the pneumonia, all these call for a liberal yet cautious use of alcohol, supplemented, of course, by the drugs already mentioned.

The same is true of marked delirium apart from alcoholism. This symptom nearly always calls for alcohol when it occurs after the first two or three days. Delirium at the outset of an attack of pneumonia may depend upon individual peculiarity and have little significance. The routine practice of applying an ice-bag to the head in every case in which there is active delirium is scarcely to be commended. Not seldom the cerebral excitement is the result of anæmia or ischæmia of the brain, and it will then be made worse instead of better by the application of cold.

Very large quantities of alcohol are sometimes given with good effect in apparently desperate cases. It is remarkable that no intoxicating effect is produced by an amount that would overwhelm a person in health not habituated to its use. It seems scarcely possible that the benefit in these cases comes from the stimulant effect alone. It is more likely that the alcohol acts directly upon the microbe by mingling with the medium in which it grows, or that it has an antidotal effect upon the poison already in the circulation.

Squire[79] reports a case of pneumonia occurring in hospital practice in which the patient became apparently moribund and was given up as hopeless. Brandy was given steadily by the interne and nurse until in twenty-four hours thirty-two ounces had been taken with decided benefit. By following up this treatment the patient recovered.

Abbott[80] reports a case of double pneumonia in a young woman of eighteen years, the lower half of both lungs being consolidated. All nourishment was refused, even milk, but she was induced to swallow brandy properly diluted, and was carefully watched for any evidence of overstimulation. Sixteen ounces of brandy were given her daily for three successive days. On the fourth day whiskey was substituted, and of this she was given twenty-four ounces daily four days in succession without evincing symptoms of discomfort or overstimulation. On the morning of the eighth day she was much improved and refused absolutely to take further stimulants. These were, therefore, discontinued, and she then took milk and other light nourishment without objection and made a prompt and complete recovery.

I have myself employed very large doses of alcohol in several cases and sometimes with marked benefit.

Digitalis in recent years has held a prominent place in the treatment of pneumonia. With the recognition that the chief danger is from heart failure, it is natural to expect benefit from the use of a drug that is of such great service in cardiac diseases in restoring the rhythm of the contractions, reducing their frequency, and giving them greater force and efficiency.

But the mechanical conditions in the two affections are as different as is possible to imagine, and the action of digitalis as an arterial constrictor, which in the one case is so beneficial, serves in the other case only to add to the labor of the organ which we are striving to sustain. Theoretically, then, digitalis scarcely seems to be indicated, and practically, while it is much employed, we have little or no evidence that it is useful as generally administered. Personally I do not resort to it unless there is cardiac arrhythmia, when I have sometimes found that the pulse became regular under its use. On the other hand, I am positive that I have often seen distinctly harmful results from its exhibition, at first in my own practice, and later in the practice of others. I have seen the evidences of dilatation of the right cavities become more marked, the lips more livid, and the chest râles more abundant; and I have seen these conditions subside when the digitalis was withdrawn, and its effects upon the peripheral circulation counteracted by the free use of nitroglycerin. Indeed, with my present views I consider the use of the drug in pneumonia without the simultaneous employment of an arterial dilator a highly dangerous and indefensible measure, and one that has contributed in no slight degree to the fatality of this disease.

Sturges and Coupland[2] remark: "For ourselves we desire to say that having used it frequently in pneumonia when in want of a cardiac stimulant where there was much dyspnœa, cyanosis, and other signs of auricular distention we have not found digitalis efficacious in removing those symptoms."

Larrabee[81] remarks that digitalis stimulates a weak heart by contracting the arteries and arterioles and throwing the blood back upon the heart itself. If there is no pulmonary obstruction the action is prompt and efficient, but the very condition which is killing the patient in pneumonia is rendered still more dangerous by such an agent.

Nevertheless, in the past ten years there has accumulated evidence to show that digitalis employed by a peculiar method may be of service in pneumonia. Beginning in 1888, a series of articles have been published by Petrescu, of Bucharest, in which he advocates the use of enormous doses of digitalis leaves, and claims for the method results that far surpass those of any other plan of treatment yet suggested. His daily dose reached the startling figure of 60–120 gr. of

the dried leaf. So far from any poisonous effects resulting he claims that in nearly every case a very prompt and decided amelioration of all the symptoms takes place, and that in six hundred cases the mortality has been less than two per cent.

Belotti and others have published articles confirming the result obtained by Petrescu. Such a remarkably successful treatment, and withal one so easily carried out, should, it would seem, have received universal favor. Admitting its claims to be well founded, we must seek a rational explanation first of the impunity with which such large doses are taken, and second of the beneficial effects obtained. As to the first point, it is to be observed that the preparation of digitalis employed is the infusion. Recent investigations show that of the four active principles obtained from digitalis, viz., digitalin, digitoxin, digitonin, and digitalein, the first is almost insoluble in water, the second quite so, while the other two are freely soluble in this menstruum. All are soluble in alcohol. Now in an infusion prepared without the addition of alcohol, such an infusion, for example, as that of the British Pharmacopœia (the United States Pharmacopœia prescribes ten per cent. of alcohol), there is a very small amount of the digitalin and no digitoxin, while the full amount of the digitalein and digitonin contained in the leaf is represented. Digitalin seems to possess to a remarkable degree the power of contracting the peripheral vessels, since Porter found that the capillary circulation in the web of a frog's foot was completely arrested by the application of a solution of 1:30,000. It is probably this principle, therefore, that gives to digitalis its power to raise the blood pressure. Its exclusion to a large extent from a purely watery infusion would therefore lessen the injurious effect that would otherwise result from the increased labor required of the heart to overcome increased peripheral resistance.

Digitoxin is supposed to be the most poisonous principle contained in the leaf. To its action is probably due the vomiting so often excited by the tincture or other preparations containing alcohol. Its beneficial action, if it possesses any, is not yet determined. It seems, therefore, that the remarkable effects obtained by Petrescu may fairly be attributed to the digitalein and the digitonin which the watery infusion contains. That this preparation will act to steady an irregular heart, and to give force and efficiency to the beat, as well as to increase the flow of urine is a matter of frequent observation. In a case of cardiac dilatation now under treatment by the writer the arrhythmia was excessive and the pulse extremely small, while the daily excretion of urine was only twenty ounces, yet under six daily doses of two drachms of the watery infusion the rhythm was

nearly restored, the pulse became larger and stronger, and the urine increased in two days to seventy ounces.

Statistics from military sources, like those of Petrescu, are open to this fallacy that the conditions, at least in time of peace, are peculiarly favorable for recovery. In Continental European armies the soldiers are all young men from eighteen to twenty-five years of age. Men recover in larger proportion than women to begin with, and younger men more frequently than the average subject. The soldier is not likely at his age to have damaged kidneys or an impaired heart as something acquired after entering the army, and before that time such a condition if present would prevent his enrollment. The same is true of syphilis and other cachexiæ. The subjects of the disease, therefore, are almost as if they were selected with reference to their ability to resist an attack of pneumonia. But this is not all. Garrison duty is irksome, and the young recruit is glad to escape from it on the slightest pretext of illness. Hence at the first symptom he reports to the surgeon, and the hospital is immediately at hand to receive him. This secures the advantage of early treatment and avoids the dangers of removal to a hospital after the disease is in progress. How potent the last two factors are may be judged from the statistics of the United States army, which being maintained by enlistment and reënlistment contains many men past the middle period of life and many alcoholics. Yet despite these unfavorable conditions and the hardships of frontier campaigning and Indian fighting, pneumonia is only about one-third as fatal in military as in civil practice.

Taking all those points into consideration, we should expect a very low rate of mortality from pneumonia in Continental armies in time of peace. Yet with allowance for all this, the results obtained by Petrescu are remarkably favorable, and it is singular that the special advantages of his treatment have not won for him a more enthusiastic support.

It is only fair to say, however, that other observers following his plan have not attained his success. Havas,[62] for example, has given the method a trial and reports against it.

Application of Cold.—The high temperature attending many cases of pneumonia naturally suggests the use of cold applications either locally to the chest or to the surface generally. But the popular idea that pneumonia is usually if not always the result of catching cold, and the resulting prejudice against what would be considered a repetition of the exciting cause, have prevented its use to a great extent in private practice and even in hospitals. And it must be admitted that theoretically a long-continued impression of cold upon

the surface, contracting the peripheral vessels and forcing the blood into the interior, does not commend itself as a plan of treatment in a disease in which vitally important internal organs are already engorged. Nor does the result of practice favor such a use of cold with the idea chiefly of reducing the temperature. In fact, experience shows that when pneumonia occurs in the course of typhoid fever, the bathing, which before was not only well borne but was obviously beneficial, becomes a source of danger unless employed with the utmost caution. But these considerations do not apply to the local application of cold in proper cases, nor to its general application in such measure as to insure a prompt reaction with accompanying nervous stimulation and more active cutaneous circulation.

Already in 1888 Liebermeister upheld this method, and showed that when properly applied it not only was devoid of the dangers formerly attributed to direct refrigeration of the surface, but that the patient breathed more deeply, expectoration was freer, and a beneficial nervous stimulation resulted. The bath was usually given at 68° F. and was ordered when the temperature reached 104° F. The duration of the bath was about ten minutes. Cold sponging was resorted to between the baths if the temperature showed a tendency to rapid increase. He referred to one hundred and fifty cases treated by him in this way at Basle, with a mortality of ten and a half per cent. as against twenty-five per cent., his average under the older methods.

A case treated with cold sponging at the Presbyterian Hospital is illustrated by the chart on opposite page.

Different observers, and especially Mays, have found marked benefit from the use of ice bags or ice poultices to the affected side of the chest. The effect of these applications cannot be directly to lower the temperature of the diseased structure. Gilman Thompson has shown that ice applied to the surface of the abdomen does not sensibly affect the temperature of the corresponding interior surface of the abdominal wall. Much less could ice in contact with the chest, although affecting to some degree the general temperature, be expected to abstract an appreciable amount of heat from the underlying lung. But this does not preclude a reflex influence that may affect powerfully the vascular action in the organ involved, as it is well known that the supply of blood to a viscus may be controlled to a marked extent by impressions produced within areas nervously related to it. In any case, there is abundant clinical testimony to the value of cold applied in this manner. The results of a collective investigation instituted by Mays,[83] and covering one hundred and ninety-

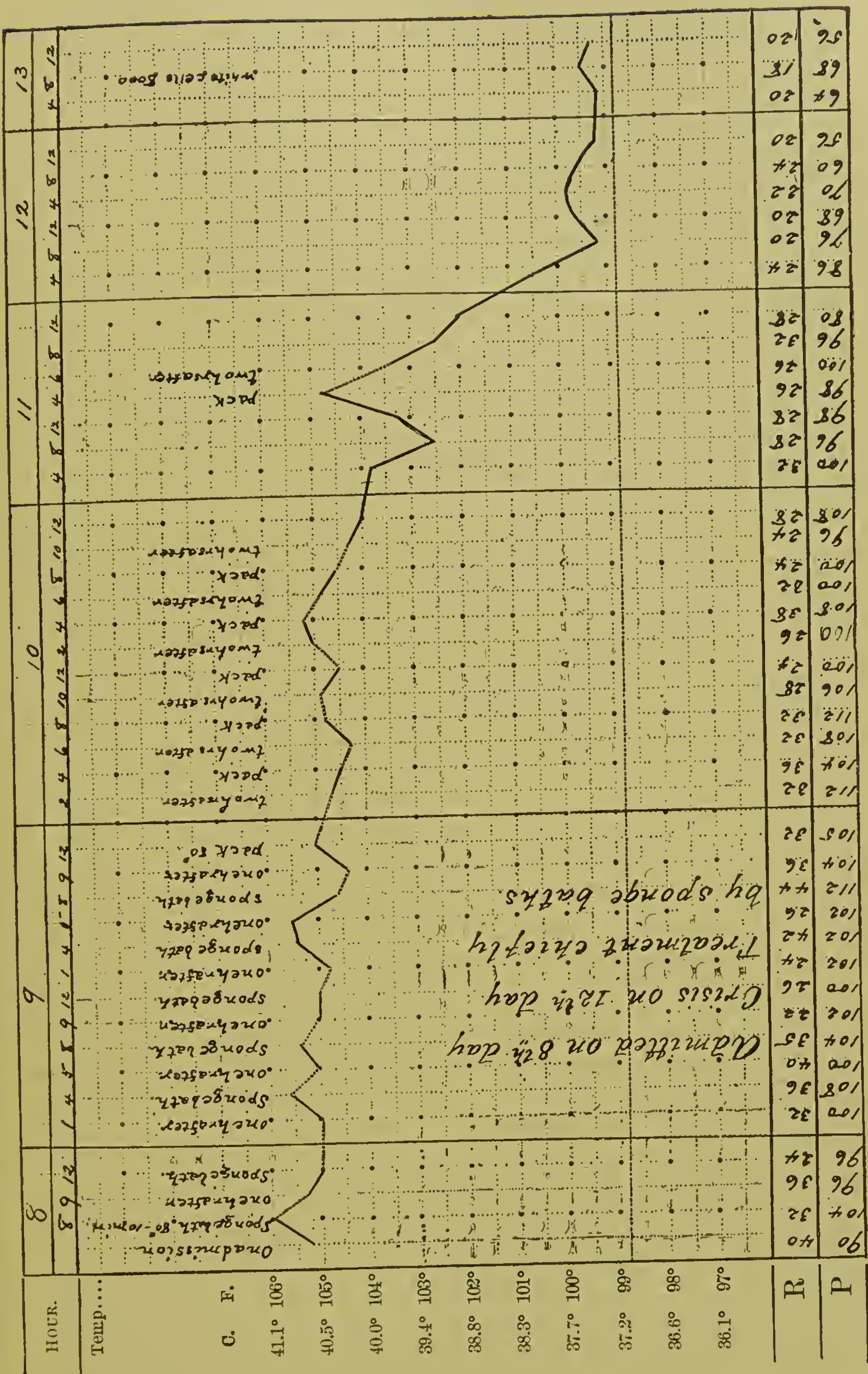

CHART No. 7.

five cases, however, had to do with private practice, where the mortality is relatively small. The figures are not therefore so favorable as they appear to be at first sight.

The method consists simply in packing bags, filled with chopped ice and covered with towels, about the affected side of the chest. The pain is relieved, the breathing becomes deeper and less frequent, the temperature and pulse decline, delirium ceases, and a general improvement begins, which in most cases is permanent.

The general application of cold, however, has its modern advocates. Baruch,[84] following Liebermeister, advises the cold bath or the cold pack, but so administered as to arouse the nervous system and stimulate the cutaneous circulation rather than with a view to direct reduction of temperature. The bath, therefore, is of short duration, and is accompanied by brisk friction, or if the pack is used, blankets are placed outside, so that the impression of cold is quickly followed by reaction and perspiration.

Peabody[85] considers the use of the tub bath precisely as in typhoid fever as marking the most important advance in the treatment of pneumonia for many years. My own experience in this line is limited to the use of the wet sheet about the trunk. In a number of cases this has seemed to be serviceable.

Antipyretics.—From what has gone before, it will be seen that there is not much room for antipyretics simply as such. The cases are rare in which benefit can be expected from merely forcing down the temperature by the use, for example, of the coal-tar preparations. Yet when with hyperpyrexia there are great discomfort and much nervous disturbance, such as headache, jactitation, insomnia, delirium, etc., and there is a fairly good condition of the pulse, one of these agents may be cautiously employed, its use being suspended so soon as a measure of relief has been obtained. The main thing is not to follow the indications of the thermometer alone, but those afforded by the general symptoms plus the thermometer.

The high temperature is not of sufficient duration to threaten of itself the integrity of the heart fibre, as it does in the case of a continued fever. The risk is from the local action of the toxin, and we add to this risk when we resort to antipyretic drugs. We are thus confined to a discriminating choice of evils.

As to which of the coal-tar products is to be preferred, while phenacetin is much in use, my personal choice is acetanilid. A combination of three grains of this and a like quantity of Tully's powder has given me much satisfaction. The small amount of morphine intensifies the soothing effect, and with the camphor acts as a stimulant to the heart, and at the same time tends to promote the action of the skin.

Relief of Pain.—When the pain is severe, nothing else will take the place of a properly apportioned dose of morphine given hypodermatically. It not only relieves the suffering, but it promotes deeper, slower, and more efficient respiration, and thus lessens the tendency to capillary stasis in the affected portion of the lung. But large doses are to be avoided, and it should be used very cautiously when there is any considerable loss of respiratory surface or any tendency to somnolence. A quarter or a third of a grain will usually be enough, and the dose may be cautiously repeated. In a doubtful case it may be more safely used in combination with a full dose of caffeine.

If in any case the use of morphine is deemed inadvisable, the pain may be alleviated by the application of an ice bag or ice poultice. In sthenic cases wet-cupping, or the application of a dozen leeches, may accomplish the immediate purpose, and at the same time exert a favorable influence on the progress of the disease. When the pain is less severe the application of dry-cups, sinapisms, etc., may suffice. Poultices, formerly so much used, are now less in favor. They are mussy, troublesome to apply, apt to become cold and clammy, and unless in the hands of a very faithful and assiduous nurse, are likely to do more harm than good. Even the time-honored oiled-silk jacket is now seldom seen, and will doubtless soon become obsolete. The jacket, made by quilting cotton batting between thicknesses of cheese-cloth, has the negative merit of being comfortable and cleanly, and is at least unobjectionable.

When the pain is low down, a single broad strip of adhesive plaster, drawn tightly around the affected part, allowing the ends to extend an inch or two beyond the meridian line, will give very marked relief. Higher up, where the movement of the ribs is less, this expedient is less useful, but it is still not entirely without benefit.

Relief of Cough.—In some cases the cough is out of proportion to the material to be expectorated, and exhausts the patient with no corresponding benefit. Worse than this, convulsive coughing tends to aspiration of the sputum into the unaffected portions of the lung, thus increasing the area of infection.

For both these reasons it is important that an irritative cough should be held in check. This may be accomplished by the moist inhalations already mentioned; but if these are not sufficient, small doses of codeine or morphine will be required. The new drug, heroin, which is a substitution-product of morphine, seems to have a special power to control cough, while not producing in the same degree the other effects of the parent drug. In doses of about gr. $\frac{1}{16}$ it has

given me great satisfaction, a single dose sometimes moderating the cough for several hours.

Œdema of the Lungs.—The supervention of pulmonary œdema during the progress of pneumonia is a very grave occurrence. It is indicated by abundant coarse râles over the whole chest, very rapid and superficial breathing, frequent and small pulse, more or less cyanosis, and profuse and often cold perspiration. It may appear with comparative suddenness, and be very promptly fatal, the patient dying of suffocation.

The treatment must be prompt and vigorous. The chest should be covered with dry-cups, or enveloped in a huge mustard poultice. A small hypodermic injection of morphine, not more than gr. $\frac{1}{8}$, will do more than anything else to restore the pulmonary circulation and check the excessive secretion, which sometimes wells in white or pinkish foam from the mouth and nostrils. In the same injection should be included gr. $\frac{1}{25}$ of nitroglycerin and gr. $\frac{1}{20}$ of strychnine. Oxygen if obtainable should be given freely by inhalation. Half a pint of very strong hot coffee should be thrown into the rectum. By these means some apparently desperate cases may be carrried through successfully. As a last resort, artificial respiration may be employed to aid in pumping the air and oxygen into the lungs.

Résumé.

In the view of the writer, the treatment of pneumonia should embrace the following points:

An attack upon the pneumococcus through the medium of the blood, the object being that the exudate when it escapes into the air cell shall be impregnated with a substance that will unfit it to serve as a culture medium.

Stimulation of the emunctories to throw off the poison as it forms.

Sustaining the vital powers and particularly the heart—cardiac stimulants.

Relieving the pulmonary circulation—vasodilators, venesection.

Compensation for loss of respiratory surface—inhalations of oxygen.

Reduction of excessive temperature—cold to surface, antipyretics (?).

Relief of incidental symptoms.

Antitoxin Treatment.

In all probability the pneumonic process as we see it from the moment of invasion to the crisis implies infection by the agency of a continually changing set of microbes. Welch has shown that the

virulence of the pneumococcus is inversely as its age, the organisms taken from the centre of a pneumonic focus having very little potency, while on the edge of a patch which is still spreading they are most active. From this we infer, and the inference is supported by the behavior of artificial cultures, that the infection of the system is not maintained through the whole period of pyrexia by the same microbes, but by a constant succession, the older ones becoming inert, and fresh once carrying on the work of supplying the toxin. This supply fails soon after the local process has ceased to spread, simply because there are no longer any young bacilli to maintain it. But while it would seem as if this might afford a sufficient explanation of the phenomena of defervescence by crisis, yet the observations of the Klemperers and others make it reasonably certain that there is an antitoxin produced that has its share in the result. Whether this antitoxin is the product of the pneumococci or is simply the result of changes going on in the leucocytes preparatory to their disintegration is not yet determined. We are apt to think of the process of absorption by which resolution is ultimately effected as beginning *after* the crisis, whereas it is in operation from the first moment of the disease, as is shown by the early infection of the general system which it brings about. Up to the point of consolidation the rate of deposition is far greater than that of removal, and a rapid accumulation of exudate takes place in the air cells. This exudate, however, is not permanent in constitution. It immediately begins a process of change, and as we have seen, the organisms contained in it change their properties also. As time goes on, there comes a period when the deposition of fresh infective material is less active than the absorption of that which is older. At this point an antitoxic effect becomes apparent, and in the cases terminating by crisis, a rapid fall of temperature takes place. In the cases terminating by lysis, either the deposition of fresh material is protracted by the invasion of new territory, or the absorption of the older material is for some reason less active.

As early as 1888, Netter rendered mice and rabbits immune to pneumonia by injecting them with fluid prepared from the dried spleen of infected animals. Later he experimented with an old pleuritic exudate containing pneumococci, and at last the sputum of a pneumonic patient, which had ceased to be virulent after the crisis.[66]

Pursuing this line of investigation, Foà found that the injection of an attenuated culture of the diplococcus of pneumonia into an animal gave immunity against the disease for several months. He produced the injection serum by precipitating the culture broth con-

taining the diplococci with ammonium sulphate and filtering repeatedly. The filtrate was injected into the veins of rabbits daily for three or four days. Subsequently he made an extract of the muscles and viscera of a rabbit which had died from pneumonia, precipitated it in the same way, and found that it gave the same immunity. The extract from a healthy rabbit when injected gave no immunity.

He next turned his attention to the immune animal, drawing the blood and allowing it to coagulate, when the serum was used to inject another animal. This also became immune. As a control experiment, he injected a rabbit with blood from a man dead of pneumonia; death resulted. He states that several species of virus are formed, one seeming to act on the nervous system, another on the blood and tissues.

The Klemperer brothers verified these results.[87] Their report is briefly as follows: Two rabbits were injected each with 20 c.c. of pleuritic exudate taken from a pneumonia patient and which by culture was shown to be free from living bacteria. Fourteen days later both were inoculated with a virulent culture. Both survived, while the control animal died. Later, they immunized animals with pneumonia sputum taken before the crisis and heated so as to destroy the poison. The same result was obtained by heating to 60° C. a glycerin extract of pneumococci. The bacteria were washed from agar cultures with sterilized glycerin, which was exposed to heat for one or two hours and filtered repeatedly. They found that immunity resulted from doses proportioned in quantity to the strength of the preparation. It was employed subcutaneously.

They found further that dogs can be immunized against pneumonia, and can also be cured of the disease. This cure takes place through the serum of immune animals, immunized by taking in the products of the activity of the pneumococcus. This immunizing serum does not cure by killing the cocci in the system, for after four days' contact with the serum the bacteria injected into an animal caused death. In fact, the bacteria in contact with this serum increase in number. At the same time the serum if injected prevents the formation of the poison in the body of the animal. This may be explained in one of two ways, either the serum hinders their power of forming poison, or the cocci go on forming poison, and the serum counteracts its effects, or through chemical changes renders it inert. At any rate, the cocci become harmless to the animal, their evil influence being destroyed by the reaction of the body cells, especially the white blood corpuscles.

If pneumotoxin and curative serum be mixed and injected into an animal, there is no rise of temperature and no effect from the

poison, while toxin alone kills the animal, with symptoms of septicæmia.*

They next inquire whether the pneumonia cured in animals by the serum is identical with pneumonia in man. Their autopsies in animals dead of pneumotoxin injections did not show the fibrinous exudation in the lungs characteristic of pneumonia, but diplococci were found in the blood. However, it is not the pneumococci themselves, but the poison that they produce that gives the septicæmic symptoms. This poison when formed at the seat of injection reaches the blood sooner than the cocci themselves. Also if we filter out the cocci, the poison remaining in solution kills the animal injected as effectually as the original culture.

In contradistinction to animals, man is only slightly susceptible to the pneumococcus. Living cocci can exist on healthy mucous membranes without doing harm, and are found in the sputum of healthy men. If we inject men subcutaneously, what results do we get? The Klemperers experimented by injecting themselves, and found that no reaction resulted from small amounts; from larger ones a local swelling with rise of temperature and febrile symptoms resulted, passing away in a few days. Hence, they conclude that men are much less susceptible than dogs to the same relative doses.

They conclude that in man it is not the exudation in the lung that renders the disease so grave, but the general infection from absorption into the circulation acting on the heart and vital centres and producing febrile symptoms. In the animals injected, the poison enters the blood stream directly and produces fever at once. The poison increases for some days, and then antitoxin is produced and immunity results. Serum taken from pneumonic patients after the

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* In this connection may be mentioned the observations of Fochier of Lyons, who recommended the production of abscesses by subcutaneous injections of turpentine in certain cases of puerperal infection. This recommendation was carried out in pneumonia by Lépine and others with gratifying results. Pinna[26] in observations already referred to (see page 44) shows that pure sterile pus has an antitoxic effect in pneumonia, and that this may be made available by Fochier's method, viz., the injection of 1 c.c. of essence of turpentine beneath the skin, thus inducing the formation of a sterile abscess. He treated in this way a patient, fifty-five years of age, suffering from apyretic and adynamic pneumonia of seventeen days' standing, in whom the diagnosis was based upon physical signs and the presence of pneumococci in the expectoration. The day following the injection the pulse rose. The temperature went suddenly up to 102.2° and the dyspnœa was relieved. Within a few days the temperature fell again to normal, and the pulmonary phenomena subsided. Meantime an abscess had formed at the site of the injection which when opened gave issue to 50 c.c. of perfectly sterile pus.

While this practice is not likely to find many imitators, the observation is of value in the discussion of the phenomena of antitoxin production.

crisis is found to cure pneumonia in dogs. They conclude that from pneumotoxin in man is produced antitoxin at the time of the crisis, and this counteracts the effects of the toxins. Thus the so-called crisis in man is the beginning of the formation of the antitoxin, and though the cocci remain for some time in the blood they are no longer harmful.*

They then question whether immunity in man results after the crisis, and conclude from researches and experiments that it does occur, but is only temporary.

With regard to the treatment of pneumonia, they say: At present we use supportive measures, awaiting the formation of antitoxin. But the aged and weak succumb. They suggest that by using the immunizing serum from animals, we may hasten this process and save lives. They have treated some cases in this way with apparent benefit, as shown by fall of temperature and slowing of pulse and respiration. But not enough have as yet been treated to arrive at a definite and final conclusion as to the value of the treatment.†

An important discussion on this subject took place at the Academy of Medicine in Turin, December 2d, 1892.[68]

Lara, chief physician of the Hospital San Giovanni, reported the results of ten cases of pneumonia under serum treatment. Five of these cases were double, five single. Eight of the patients were young persons, two advanced in years; six were robust, four of debilitated habit. The serum was in some cases from immunized rabbits, in other cases from dogs, and in still other cases a glycerin extract made from the viscera of refractory animals was employed. In no case was there any local reaction. The glycerin extract produced no observable general symptoms. Serum from dogs caused nervous excitement; that from rabbits produced general agitation and a temporary aggravation of the disease. In all but three cases there was reduction of temperature, not sudden, but after an interval.

A change in the character of the pulse was observed without a reduction in the number of beats. There was no immediate change in the respiration, but after a time it became somewhat slower. The crisis took place in from three to five days. The convalescence was rapid and complete; complications were rare and of little gravity. The reporter considered the results encouraging.

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* This statement is not in accord with more recent observations which show that cases in which cocci are found in the blood generally prove fatal.

† Pana and di Renzi, of Naples, have produced a serum by inoculating animals with pneumonia bacilli, and have employed it in some 32 cases with 29 recoveries and 3 deaths. In respect to all of the latter the autopsy showed the presence of other diseases of a fatal nature. Maragliano experimented with this serum in five cases with success in all (Antonio Fanoni[67a]).

Bozzoli reported five cases treated with serum from rabbits prepared by a special process not described. There was rapid fall of temperature in every instance. Four of the patients recovered and one died after defervescence. The kidneys were unaffected.

Di Renzi reported that during the past year he had treated ten cases of pneumonia with antipneumococcic serum, prepared as follows: The animals were inoculated with a non-lethal quantity of pneumonia virus, the dose of which was gradually increased until a strong immunity was produced. Serum from these animals was injected into the patient. Only severe cases were selected for treatment. In every case cure resulted. In one case the temperature came down on the third day, although there were signs of diffuse hepatization. Of five other cases admitted during the year, and not treated with serum, one died. Although the author admits that his cases might have recovered without the serum treatment, he considers his results decidedly encouraging, as pointing to a real and efficient treatment of pneumonia.[89]

Wiesbecker[90] reports five cases of pneumonia treated with injections of serum obtained from patients recovering from the disease. While there was no uniformity in the results so far as the objective signs were concerned, these becoming more and more severe in some cases after the injection, while in others the severity abated, there was in every instance a most remarkable improvement in the subjective conditions. This improvement was almost instantaneous, in one case being manifest within one and one-half minutes after the injection. But for one instance in which the patient was a child only three years of age, we should be inclined to refer these marvellous results to suggestion, especially as they did not conform to the physical conditions present at the moment. Difficulty of breathing, pleuritic pain, malaise of every description disappeared as if by magic; recovery took place in every case, though not always with remarkable promptness. The quantity of serum in each case was 10 c.c.

Similar to this was the experience of Fourriere[91] in a single case treated by injections of goat's blood. The patient, a person past middle age, was recalled to life from an unconscious, fairly moribund condition, and though death occurred after several days, there was an interval during which danger seemed to be over and recovery assured.

In 1897, Washbourn, of Guy's Hospital, published his researches on antipneumococcic serum. His method was essentially that employed in producing diphtheria antitoxin. A pony was the animal selected, and after nine months' treatment, first with living and then

with dead cultivations, the serum was found to possess marked protective powers. By using a special method of cultivation, it was found possible to maintain the virulence of the pneumococcus at a given level for a period of sixty-six days. To maintain the virulence of this culture it must be kept in an incubator at a temperature of 37.5° C. He claims that under these conditions the antipneumotoxin can be accurately standardized.[92]

Several cases of pneumonia have been treated by Washbourn and others with this serum. While its influence cannot be distinctly traced, it can be fairly considered to have contributed to the favorable result in some extremely unpromising cases.

We cannot avoid the conclusion from this résumé of the achievements of orrhotherapy in its application of pneumonia, that up to the present time they can scarcely be said to amount to more than an encouragement to further effort. No really decisive results have been obtained. In some cases the effect seems to have been favorable, but in view of the variable course of pneumonia under all forms of treatment, it is impossible to assign to the injections any positive share in the result. It can be only by the accumulation of a large number of observations that a conclusion as to the value of the treatment can be arrived at, and, unfortunately, the difficulties in the way of extended observation are such as to deter most investigators from pursuing the subject.

The first difficulty is found in the short life of the pneumococcus and its feeble power of resistance. Cocci that are virulent at the beginning of an investigation cease to be so as the investigation proceeds. On the other hand, toxins that are expected to produce only a moderate reaction when injected sometimes display an unlooked-for virulence. Animals apparently progressing normally towards immunity most unexpectedly succumb to septicæmia from a dose of toxin supposed to be entirely within the limits of safety. Again, animals that were readily immunized at first lose their immunity in spite of renewed inoculations, and the serum obtained from them ceases to be reliable. This variation in the conditions under which experimentation is conducted is liable to vitiate the most carefully drawn conclusions. If this be true under the favorable circumstances of the laboratory, what must it be in the exigencies of ordinary practice? If before employing a therapeutic agent we must resort each time to experiment to test the value of the specimen in hand, the usefulness of the agent will be very limited.

It is to be hoped that this difficulty has been overcome by Washbourn's method already mentioned, and that it will be possible in the future to command a supply of reliable antitoxin for the treatment of

pneumonia, as we already do for the treatment of diphtheria. Efforts to produce such a supply are now being made by the Health Board of New York. Should they be successful, the value of the method will soon be determined.

Both Bonardi and Griffiths succeeded in isolating crystallizable substances which were supposed to represent the active principle of the pneumotoxin, the first from cultures in artificial media, and the second from the urine of pneumonic patients. But their conclusions seem to have been negatived by subsequent investigations carried out at the Institute for Experimental Hygiene at Rome, by Alfredo Andreini,[93] so that we are still ignorant of the chemical properties of the poison, and as far as ever from the brilliant therapeutic results which it was thought were about to be realized.

Pneumonia in Childhood.

Pneumonia in childhood differs in some respects from the disease as occurring in adults.

As young children do not expectorate, the study of pneumonia in them is deprived of the aid to be derived from the examination of the sputum, so useful in the case of older persons. As most cases end in recovery, the opportunity for autopsical research is limited. For these reasons our knowledge of pneumonia as it occurs in childhood is relatively incomplete.

In the Kaiser und Kaiserin Friedrich Kinderkrankenhaus at Berlin, Schlesinger found that in children up to fourteen years of age genuine fibrinous pneumonia occurred in the proportion of thirty-seven to two hundred and seventy cases of bronchopneumonia. Holt[93a] states that after three years of age nearly all primary cases of pneumonia are of the croupous variety. During the first two years twenty-five per cent. of the cases are croupous and seventy-five per cent. bronchial.

Croupous pneumonia appears in earliest childhood, it has been even recognized at birth. It attains its greatest frequency in the fourth year, after which the morbidity decreases until puberty. From earliest infancy, when the mode of life is the same in both sexes, boys are more frequently attacked than girls, in the proportion of eleven to seven (Schlesinger,[94] Morrill[95]). Children of vigorous constitution are not more exempt from attack than the less robust. Zymotic disease and acute gastritis play an important part as exciting causes. The season of the year has the same influence as in adults.

Symptoms.—In about half the cases the attack begins with vomiting; in about seven per cent. with convulsions (Holt).

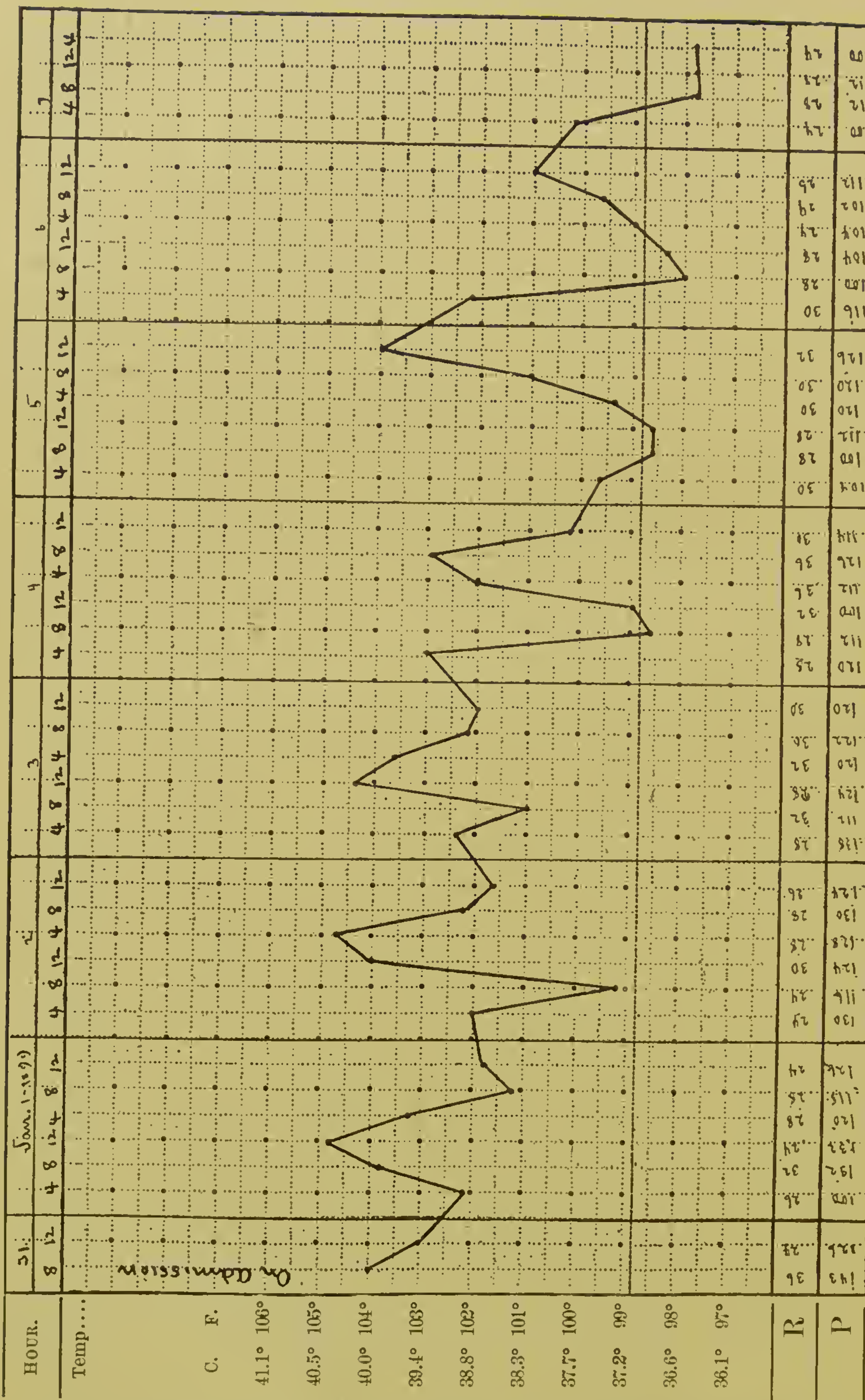

CHART No. 8.—Showing the Intermittent Temperature Quite Common in Children.

As a rule, the younger the child the higher the *temperature* range, and the more frequently the fever assumes an intermittent or remit-

tent form, contrasting in this with the comparatively even temperature observed in the adult. In pneumonia of the upper lobe the fever generally is higher and more constant than when the lower lobe is the seat of the disease; but there are exceptions to this rule, as in the case of which a chart (No. 8) is here presented. Morrill[96] found the highest temperature in seventy-two cases to be 106.5° F., lowest maximum 101° F. Average critical day in fifty-four cases, the eighth.

As compared with adults defervescence by lysis occurs less frequently in children, in proportion as the pneumonia is purely lobar and not bronchial, and the fall of temperature at the crisis is more marked. Especially in very young children, and in disease of the upper lobe subnormal temperature after the crisis is the rule, sometimes to the extent of 2° or 3° F.

Procrisis as distinguished from pseudocrisis appears to be a peculiarity of childhood.

While the disease is at its highest the temperature, pulse, and respiration remain nearly parallel with each other. At the crisis, the first two fall abruptly, while the respiration sinks more gradually. After the crisis the relative frequency of pulse to respiration not uncommonly falls below 2 : 1°. This, in children, is very rarely the case before defervescence. Excessive rise, the pulse, for instance, above 170 and the respiration above 75, is rare in croupous pneumonia, as is also a slowing of the pulse to below 80 after the crisis is past.

The lesion of croupous pneumonia does not observe the boundaries of the lobes nearly so accurately in children as in adults. Much more frequently the invasion of a neighboring lobe remains only partial. Dulness on percussion is more marked than the auscultatory signs, and will often be apparent in cases that without it would be overlooked. It is never safe to exclude pneumonia in a child simply because we fail to get bronchial breathing and bronchial voice. The percussion should be light and with a single finger.

Holt observes that when the appearance of physical signs is delayed, we should look for them in the axillæ and in the mid-clavicular regions in front.

Double pneumonia is less frequent in children than in older persons, while an attack limited to a single upper lobe is relatively common. When several lobes are invaded it is usually in succession, and there is an ascending scale in the severity of the attack. In twenty cases observed in the New York Foundling Hospital* the

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* Private note from Dr. Kauenhoven.

right lower lobe was primarily involved in seven, the left lower lobe in eight, the right upper lobe in three, the left upper lobe in two.

The age of the youngest child with distinct signs of lobar consolidation was five months. There were three cases in children six months old and under. In all cases with only one lung involved defervescence took place on or before the sixth day. All uncomplicated cases terminated in recovery. Of the two fatal cases one was complicated with rachitis and one with croup. Both were in children under one year of age.

Morrill[96] gives the location of the lesion as follows: right middle or lower lobe, 40 per cent.; left lower, 25 per cent.; right upper, 10 per cent.; left upper, 8 per cent.; right apex, 5 per cent.; left apex, 4 per cent.; both lungs, 5 per cent. Mortality, 5 per cent.

Resolution progresses more rapidly than in average cases in the adult. Unresolved pneumonia is rare, and the issue in gangrene or in phthisis is almost never encountered.

The normal course of pneumonia in childhood is more severe than in adult life. Right-sided cases are more severe than those on the left, but pneumonia of the upper lobes is not more serious than that of the lower. After a prodromal stage of one or two days which in children is not infrequent, the disease develops without marked initial symptoms. These, however, are seldom wanting when the attack is sudden and without prodromes. A pronounced chill is much less frequently observed than in grown persons (Morrill found it present in only five per cent. of one hundred cases), while vomiting is very common. Convulsions are rare and occur for the most part only in very young children, and in right-sided attacks. Just before the crisis the child often is much sicker than at any previous stage. The contrast then with the subsequent rapid improvement is most striking.

Still in a small fraction of cases the recovery does not begin at once with the fall of temperature, but a day or two days of exhaustion and depression intervene.

Abortive Pneumonia.—Baginsky[97] describes under this title a form in which the attack sets in suddenly, giving rise to the suspicion of croupous pneumonia by the type of the respiration, the temperature, and the pulse, and yet does not come to the full development of the physical phenomena. Rather, the process seems to be arrested halfway; before it comes to actual consolidation the fever breaks, and the morbid conditions disappear as rapidly as they arise. He considers these as undoubtedly cases of pneumonia that have retrogressed in the stage of engorgement which always precedes consolidation. In his practice such cases are not very infrequent.

Under the title of "wandering pneumonia," he observes that

while it is not very common that pneumonia spreads from lobe to lobe or invades in succession the entire lung, yet such cases do occur. By physical examination it is possible to follow these several developments. The cases divide according to the temperature curve into those in which the fever remains constant, and those in which there is a decline of temperature followed by another rise. While we have to do in the first case with a single protracted attack, the other represents the recurrent type of pneumonia in which a new section of lung is invaded. All attacks of this kind have a long duration and follow a severe course.

Baginsky also recognizes a type which he terms "gastric pneumonia." In this form the gastrointestinal phenomena are in the foreground, while the affection of the lung, until shortly before the critical appearance, assumes but little prominence. These cases are apt to begin with vomiting, and diarrhœa is a leading feature. Only when the disease has made considerable progress does the pulmonary implication appear in its true character as the essential element in the case.

Among the anomalies in the progress of the disease, an abortive action is observed more frequently in distinct but circumscribed infiltration than when only the stage of congestion is reached. The most dangerous anomaly in children is the migratory tendency. The difference in the varieties it occasions lies in the duration of the intervals between the several migrations. A recurrence of pneumonia is as rare in children as in adults, though relapses may occur and the attack is greatly prolonged in consequence. Stockton[98] reports a case in which the entire duration was sixty-eight days.

The most frequent of the abnormal developments is "cerebral pneumonia." A convulsive, a comatose, and a delirious form are distinguished. The cause of the brain symptoms may be found in the pyrexia, in the severity of the infection, in an otitis media, or finally in an individual peculiarity of the child. A genuine meningitis as a complication of pneumonia is apt to follow an almost latent course.

The examination of the blood shows that the leucocytosis follows essentially the same course in the pneumonia of children and of adults.

Complications.—A slight bronchitis is often observed in the beginning of the attack in a child, being apparently a continuation from the prodromal stage. Later it is of rare occurrence, but of more serious moment. Pleurisy is the most frequent complication, especially in pneumonia of a lower lobe. It is even more frequent than in the adult. For the most part it follows a favorable course, seldom pass-

ing into empyema. It influences the fever but little, but even when it is slight, it delays more or less a complete recovery. Albuminuria is remarkable for the relative rarity of its occurrence in the pneumonia of children. When present it is slight in amount and of short duration.

Herpes is relatively uncommon. Icterus is lighter and less frequent in childhood than in later years.

Otitis media is especially a complication belonging to childhood. Its course is generally severe, and often accompanied by cerebral symptoms. It aggravates the fever very materially. As regards the ear itself the inflammation usually runs a favorable course. Otitis occurs for the most part during the first three years of life and in cases of pneumonia affecting the right side.

Prognosis.—The mortality of pneumonia in children is markedly less than in adults, in round numbers about one-third as great. Morrill gives the mortality in seventy-two cases as 1.5 per cent. The fatal cases are largely the result of complications of which the most important are meningitis, purulent pericarditis, and bronchopneumonia. As affecting the prognosis, the constitution and, in a less degree, the age, are to be taken into account.

As to the *diagnosis*, many of the peculiarities in the course of pneumonia in childhood spring from its relation to bronchopneumonia, which has yet to be sharply differentiated from it. The secondary pneumonias are very seldom croupous.

In the *treatment* a constant progress towards greater simplicity is the modern tendency. Energetic measures are less frequently resorted to. For lowering the temperature cold packs are coming into favor as against the use of the coal-tar preparations and other internal antipyretics. While the latter depress the already weakened heart, the former, if judiciously applied, improve its innervation and arouse its flagging energy. It is, moreover, to be recognized that up to a certain point the increased temperature is a useful factor in the struggle of the organism against the specific infection, and that if it is not excessive its forcible reduction is to be deprecated. A proper use of tonics and stimulants, including alcohol, will be of service.

BRONCHOPNEUMONIA.

Lobar pneumonia in children is ever prone to take on more or less of the characteristics of bronchopneumonia, that is to say, it is apt to appear in different localities and to be accompanied by signs and symptoms of bronchitis. The distinction between the two forms is not always sharp, and both may be present at the same time.

This subject has been studied recently by Samuel West.[99] The following is a résumé of his paper:

The author believes that under the one term "bronchopneumonia" several different conditions are included, and that many of them are pneumococcus inflammations; in other words, that some of the bronchopneumonias of children are really the same disease as the common pneumonia of the adult, or to put the proposition in another form, that the only difference between the pneumococcus disease of the adult and that of the child is that in the one case the consolidation which results is lobar or massive, and in the other lobular or patchy.

Speaking generally, bronchopneumonia is shown to be associated with several varieties of pathogenic organisms; for example, the streptococcus, staphylococcus, Friedländer's bacillus, the tubercle bacillus, and others; but chief among them all is the pneumococcus, which, taking all cases together, is present either alone or in association with some of the others named, in at least fifty per cent. Thus Netter examined forty-two cases, and found:

			Per cent.
Pneumococcus alone in	10	19	= 45
With others in	9		
Streptococcus alone in	8	23	= 60
With others in	15		
Staphylococcus alone in	5	13	45
With others in	8		
Friedländer's bacillus alone in	2	6	
With others in	4		

Weichselbaum, in 15 cases, found the pneumococcus in 7, streptococcus in 6, Friedländer's bacillus in 1, and streptococci and staphylococci in 1. Horton Smith, in 11 cases, found the pneumococcus alone in 5, with others in 3—that is, in 8 out of 11, and in only 3 cases was it absent. Mosny examined 4 cases of primary bronchopneumonia, and found the pneumococcus in 3 and the staphylococcus in 1. In 13 secondary cases the pneumococcus was present alone in 1, and associated with the streptococcus in 1. The streptococcus was found alone in 5, and associated with other bacilli in 5 more. Friedländer's bacillus was present in 1, and an unknown bacillus also in 1.

So far as the evidence goes it seems to show that in secondary bronchopneumonia the streptococcus is the most frequent organism, and in primary bronchopneumonia the pneumococcus, and that among the latter the pneumococcus is almost as common as it is in lobar pneumonia of adults.

It is now well known that the microscopical distinctions often

drawn between the minute lesions of lobar and lobular pneumonia cannot be regarded as absolute, and that for example even the fibrin network which is so common in lobar pneumonia is not uncommon in acute bronchopneumonia, while it may be absent in lobar pneumonia.

The conclusions to which this evidence points are obviously these:

1. That the primary and secondary bronchopneumonias have a different bacteriological origin.

2. That secondary bronchopneumonia is for the most part due to streptococcus infection, derived from some source in connection with the air tubes, throat, or mouth.

3. That primary bronchopneumonia is of pneumococcal origin.

4. That pneumococcus inflammation occurs with almost equal frequency in the child and in the adult.

5. That pneumococcal inflammation takes a different form in each, in the adult producing massive consolidation and in the child disseminated patches of consolidation; in other words, that there are no real pathogenic distinctions between lobar pneumonia of the adult and primary lobular pneumonia of the child.

To sum up, the author is of the opinion that the term "bronchopneumonia" would be best reserved for those inflammations of the lungs which follow antecedent affections of the bronchi, and that their exciting cause for the most part will be found to be other organisms than the pneumococcus, while, on the other hand, the primary bronchopneumonia of children is really croupous pneumonia occurring in a disseminated and patchy form instead of a massive consolidation.

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CEREBROSPINAL MENINGITIS.

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CEREBROSPINAL MENINGITIS.

Introduction.

Synonyms.—Epidemic cerebrospinal meningitis has received many different names, in each of which some special feature of the disease is brought prominently forward. Thus the word *Genickstarre*, frequently given to the disease in Germany, makes allusion to the rigidity of the nucha, which is one of the most constant and characteristic symptoms of cerebrospinal meningitis. The names cerebrospinal fever and cerebrospinal typhus (Boudin) imply that the authors employing them believe that the suppurative lesion of the meninges is not the essential feature, and that we have not to do with a simple inflammation but rather with a general disease, the local lesion of which is found most constantly in the meninges. Finally the terms spotted fever, formerly much employed in America, and purpuric fever of the Irish writers, are derived from the fact of the petechial eruption frequently observed in the course of certain epidemics.

This disease has been the subject of very many memoirs, the number of which is justified by the interest possessed by the affection. Documents which must be consulted in the study of cerebrospinal meningitis have originated in nearly every country, since there is hardly one which has not been invaded by this singular malady. And yet many points in regard to the disease remain very obscure. The pathological anatomy which shows us with great distinctness the lesions of the meninges, the participation of the superficial regions of the brain and cord, the alterations in the organs of special sense, and the accompanying modifications of the other organs, has not yet enlightened us sufficiently concerning the initial changes. We do not know with any positiveness the relations between suppurative cerebrospinal meningitis sporadically occurring and that which we encounter in epidemic form. The latter furthermore is far from presenting always the same appearance, and although there is fairly general agreement in placing it among the general infectious diseases there is still discussion as to the place it occupies in this class, and there are physicians even at the present day who dispute its contagious nature. Bacteriology even, which has revealed to us many

important details, has nevertheless left more than one point still unsolved.

All these matters will be taken up and studied in their proper place in the following pages. This study I propose to undertake according to the following scheme: A. History and geographical distribution. B. Clinical study: (1) General sketch; (2) symptoms; (3) course and termination; (4) complications; (5) varieties; (6) diagnosis; (7) prognosis; (8) treatment. C. Bacteriology. D. Epidemiology.

It is impossible to give here even a simple list of the authors who have been consulted in the preparation of this article, and whose works may most profitably be consulted, and I can cite only those who excel on various points: In France the memoirs of Tourdes, of Faure Villars, and of Boudin; in Germany the monograph of Hirsch and a very remarkable study of Leichtenstern; in Ireland a remarkable report of Collins; in America the memoir of Webber and the recent report of Councilman, Mallory, and Wright. Mention should also be made of the thesis of Friis of Copenhagen and the work of Sievers on meningitis in Sweden, Norway, and Finland.

I have personally for a long time devoted much special study to this affection, especially to the bacteriology and pathogenesis. At first limited to sporadic meningitis my studies were gradually extended to a certain number of cases of epidemic meningitis, especially during the past year when a small epidemic, of which I was the first to recognize the nature, occurred in Paris.

The bibliography at the end of this article includes first the principal works of the authors just mentioned, and following them comes a list of the memoirs which have been referred to in the course of this study.

HISTORY AND GEOGRAPHICAL DISTRIBUTION.

We cannot study here in detail all the various epidemics of this singular affection, the reader desirous of this being referred to the special works of Boudin[iii],[iv] and of Hirsch,[v] the following sketch containing notes of only the most important of the great epidemics.

It would be unprofitable to inquire whether the "phrenitis" of Hippocrates and of Celsus was meningitis or whether the epidemic of Abderus of Lucian or the epidemics of the Middle Ages were of this affection. It is possible that in the seventeenth and eighteenth centuries cerebrospinal meningitis appeared more than once, being confounded with typhoidal diseases or with petechial fevers.

The authentic history of the disease, supported by the evidence

of both symptomatology and pathological anatomy, commences only with the present century, and it is at precisely this time that we find it appearing in the Old and the New World.

Epidemics from 1805 to 1816.—In Europe it was at Geneva that Vieusseux and Mathey[104] described an epidemic which broke out in the month of January, 1805, seizing first two children in a family of four persons, then four in a family of seven persons in the neighborhood. The visitation subsided in the month of May after the disease had caused the death of thirty-three persons. Alongside of very marked nervous symptoms the authors mention the occurrence of a petechial eruption. This was exactly the description given by American authors to a disease occurring in epidemic form which made its first appearance in Medfield, Mass., in March, 1806, and raged during this and the following years in this State and in Connecticut, Ohio, and Kentucky (Comstock, Woodward, and Elisha North[131]). This epidemic prevailed in various parts of the United States and Canada until 1819, and gave occasion to numerous valuable memoirs which we find very well abstracted in the work of Webber.[viii] All the descriptions of this period make special mention of the eruption (spotted fever) as well as of the nervous phenomena.

In Europe the year 1805 marked also the beginning of a period of almost the same duration, in the course of which cerebrospinal meningitis made many appearances in different points. A fact worthy of mention in these epidemics is that the nervous phenomena were ordinarily accompanied by petechial eruptions and pleural and pulmonary inflammations. Visitations of this character occurred in the Prussian army in 1806–7, among the Spanish prisoners at Brienne in 1807, at Dantzic in May, 1811, at Brest in 1813, at Mayence in 1813–14, at Grenoble in 1814 (Comte[27]), at Paris in 1814 (Biett[13]), and at Metz, Sarreguemines, and Pont-à-Mousson.

This first period of epidemic cerebrospinal meningitis did not, however, leave as deep a mark as it would had it not coincided with grave epidemics of typhus fever, with which disease the former was frequently confounded. Still less attention was paid to the less extensive epidemics during the next fifteen years, but the year 1837 marked the beginning of a second period which was much more fruitful as regards the history of epidemic cerebrospinal meningitis.

From 1837 to 1849 cerebrospinal meningitis appeared very many times in France. The disease showed a peculiar predilection for bodies of troops, respecting almost entirely the civil population, and visited all the fortresses of the country. A very peculiar fact and one that has not been noted elsewhere or at any other period was that these outbreaks were very plainly joined one to the other by a chain,

all the links of which it was possible to trace. The epidemic began in 1836 among the civil population in the Department of Landes in the Basses Pyrenées.[33, 63] Soon after it began it invaded the garrisons at Bayonne and Dax. A regiment, which was in the affected region and suffered somewhat from the prevailing illness, had some of its members fall sick in Bordeaux and others at Rochefort, where the epidemic lasted from January 15th to February 8th, 1836. The convict prison was invaded by the epidemic towards the end of 1838. At this time the regiment left Rochefort and went to Versailles. Early in February, 1839, six men of the regiment, all living in the same chamber, were attacked with cerebrospinal meningitis at intervals of a few days.[37] This regiment furnished the greatest number of cases at Versailles; some of the other regiments in the same garrison were also attacked, but less numerously. From Versailles this regiment was transferred to Chartres, and although the line here is not so easily traced, there is no doubt that the regiment carried the disease to Metz, Strasburg, and Nancy, and from these localities it was transported to Schlestadt and Colmar. At the same time that the disease was being carried from the southwest towards the northeast along the route just indicated it passed in other directions, going towards the Mediterranean and ascending the valley of the Rhone. Foix, Pamiers, Avignon, Pont-Saint-Esprit, Marseilles, Aigues-Mortes, and Lyons mark the successive stages of this journey. From 1841 to 1849 very many other garrison cities were invaded, among them Orléans, Cambrai, Lille, Nantes, St. Etienne, Bourges, and Toulon. The regiments stationed in Algeria soon followed in their turn, many of their members in the different garrisons being attacked by the disease between the years 1839 and 1847.

It seems to be fairly well established also that the cases of cerebrospinal meningitis occurring at the same time in Italy were directly dependent upon the epidemic in France. Indeed, Ancona, where the first cases were observed in 1839, had been garrisoned since 1832 by troops coming from France. Between the years 1839 and 1845 cerebrospinal meningitis prevailed in very many localities in Italy, especially in the kingdom of Naples, although not sparing the central provinces or even Piedmont. Just as we have seen that the disease crossed the Mediterranean to invade Algeria, so it passed over the Adriatic and appeared in Corfu in 1840, carried there from Sinigaglia near Ancona. During this same period we find epidemics existing at Gibraltar,[54] where it attacked almost exclusively the civil population (1844), in Denmark (1844–47), and in Ireland (1846 and 1850). America also suffered at this time, circumscribed epidemics being noted between 1842 and 1850.

Scandinavian Epidemic from 1854 to 1861.—During the period from 1849 to 1861 cerebrospinal meningitis, while it did not disappear completely, yet did not figure to any extent except in the Scandinavian peninsula,[xi] where up to that time it had been comparatively unknown. The disease invaded almost the whole of Sweden in the years 1854–61, and Norway was also attacked in 1854 but not so severely. The disease progressed here in a peculiar manner, distinguishing it from the two types presented in the first and second general epidemics. It marched progressively and almost systematically from the southwest northwards, invading each year new districts and sparing those that had been visited the year before. As a rule each of the outbreaks began in January and died out in May or June. In Sweden the epidemic was remarkable for its general diffusion, every province being invaded, with the exception of the two most westerly ones. In seven years there were four thousand one hundred and thirty-eight deaths caused by cerebrospinal meningitis in Sweden. In Norway the disease prevailed over a much more limited area.

Epidemics of 1861 to 1868.—The winter of 1861–62 marked the beginning of a new epidemic period, during which all those regions were invaded which up to that time had enjoyed a comparative immunity. Germany had generally escaped until then, although Silbergundi[161] has left us a description of an epidemic which prevailed in 1822 in a town in Rhenish Prussia, and which was followed by renewed outbreaks in 1827, 1838, 1843, and 1851. The disease appeared in Prussian Silesia in 1863. Central and Southern Germany were invaded at the same time, and the disease prevailed there up to 1866. Austria and Hungary were spared for the most part, though there were epidemics at Trieste and Pola. In Russia[157] cerebrospinal meningitis prevailed at the same time that it did in Prussia (1863–68), but it does not seem possible to establish any close relation between the epidemics in the two countries.

During the same period that the disease prevailed to a considerable extent in Germany we find no less severe epidemics in Ireland (1865–67), and in the United States, where it appeared at a still earlier period. It was first noted during the winter of 1861–62 among the troops of the Army of the Potomac. It prevailed during the following years, increasing in severity, and appeared in New York in 1863 where it remained, preserving a distinctly epidemic character, up to the year 1866.

Later Manifestations.—Since these four great epidemic periods—1805–16 in America and France, 1837–49 in France and Italy, 1854–61 in Sweden, and 1861–68 in Germany, Ireland, and the United States—the disease has returned a number of times in quite severe

form, but in general its manifestations have been more circumscribed and hardly of epidemic proportions. It would seem as though the scourge had become acclimated in certain regions, for we see that the large cities in America are almost never completely free from it, and epidemic recrudescences have occurred in New York in 1872 and in Boston in 1874 and 1896-97. Similar slight epidemic recrudescences have been noted in Cologne in 1885, in Vienna in 1886 and 1897, and in Berlin in 1896. Small epidemics have occurred in Denmark, Sweden, Norway, and Finland. In France and Italy the invasions have been less extensive, though there has been hardly a year in which the disease has not prevailed to a slight extent in some or other place in these countries.

It would appear that during the past three or four years the disease has had a period of increase, presaging a more important epidemic return in various countries.

In conclusion we may say that there is no continent and no country which has not been invaded to greater or less extent by cerebrospinal meningitis. Although Scotland, Belgium, Holland, and Switzerland have suffered but little, yet they have not escaped entirely. We may add that, outside of Europe, America, and Africa, the epidemics in which have been noted in the brief sketch just concluded, epidemics occurred in Smyrna in 1870 and in Jerusalem in 1872. Oceanica has also been invaded.

CLINICAL STUDY.

General Sketch.

While it is always difficult to sketch in a few lines the principal features of any disease, it is especially so of epidemic cerebrospinal meningitis, in which authors distinguish a number of clinical forms.

A schematic picture of the affection would be nearly the following, which corresponds to the classical description of meningitis of the convexity, "phrenitis" of the older writers.[136] A person of usually vigorous health is suddenly seized with an excruciating cephalalgia, accompanied by vertigo, nausea, and vomiting; the pain extends to the back of the neck and the spine and invades the extremities; the patient's mind begins to wander, he loses consciousness, and is the prey of a convulsive agitation; the head is drawn backwards, the face, which is red or pale, has an expression of pain; the temperature of the skin may be normal, elevated, or reduced, and the pulse is also variable in its character. This condition lasts up to the third day when an eruption develops; the urine is now turbid and constipation

is obstinate. Soon consciousness returns and with it an appreciation of the pain. A slight amelioration of the symptoms at this time often raises hopes which are seldom realized. The cerebrospinal phenomena soon return with all their acuteness, the fever rises, the tongue has a yellow coating and where not coated is red and dry; diarrhœa succeeds to the constipation. Sometimes the nervous symptoms retain their violence up to the very end; sometimes they diminish in intensity, and sometimes they persist obstinately in mild form; their progress is often broken by remissions and exacerbations. The exhaustion and emaciation make frightful progress, the fever assumes a hectic or typhoid form, and the patient expires from exhaustion after a tranquil agony. If recovery is to take place, the symptoms subside only slowly, and a long and perilous convalescence precedes the reëstablishment of health.

We have borrowed from Tourdes[1] most of the features of this sketch, as given by him in his description of the disease occurring in Strasburg. We shall see later what modifications may occur in this picture and how authors have been led to describe a certain number of varieties. But before this it will be well to study the chief symptoms more in detail, and this will be most conveniently done by examining in succession those referable to each system.

Symptoms.

We will begin our study of the symptomatology of cerebrospinal meningitis with the nervous system, which is naturally the most affected.

Nervous System.—The first symptoms are those relating to sensation, pain being one of the most constant phenomena, especially at the beginning.

Cephalalgia is never wanting. It usually begins as a frontal headache, but sometimes it is occipital; limited at the beginning to a single region, it almost always spreads later, becoming universal. It is sometimes mild, but is more frequently acute, and may even be excruciating, dragging cries and groans from the sufferer. It develops at the beginning of the disease and persists throughout its whole course; it may be temporarily hidden by delirium or coma, but always reappears upon the return to consciousness, and constitutes one of the most tenacious of all the symptoms. It is usually most severe in the evening, and light, noise, and especially movement, increase the pain. The patients often lie motionless, with the head compressed strongly between the hands, but sometimes they are subject to an uncontrollable restlessness.

Rachialgia is frequent, although not so constant as headache. It may involve the entire spinal column, but this is rare; the cervical region is the most frequent seat, after which come the lumbar and sacral regions, the dorsal region occupying the third place in point of frequency. This pain is cruelly acute, forcing cries from the sufferer. It is not increased by even strong pressure, but all movements increase it. It compels the patient to preserve an immobility which may even be mistaken for tetanic rigidity, and determines a peculiar position of the body, the head being thrown backwards on the nucha, and the spine also being extended. At other times a terrible restlessness accompanies the pains, and the patient is the subject of extraordinary convulsive movements, as if he were trying to throw off a frightful weight. In rare cases the spinal pains appear first, but more frequently they follow the headache. They are less persistent than the latter, and may present periods of remission or intermission in cases in which the disease lasts a certain time.

Pains in the limbs are less common than those in the head and back, occurring in about a third of all cases. They are located more especially in the lower extremities on their posterior surface, and more rarely in the arms. They are often accompanied by muscular contractions and cramps. The pain may have a manifestly articular localization in the shoulders or jaws, and sometimes its characters recall exactly those of acute articular rheumatism.

A very careful examination of the patients will show us in most cases the presence of *anæsthetic areas*, but this symptom has comparatively much less value than those above mentioned.

Rigidity of the nucha has been regarded by many authors as the most characteristic phenomenon of cerebrospinal meningitis. The term "Genickstarre," employed by the Germans as a synonym of the disease, indicates sufficiently the importance of this symptom. The backward curve may be limited to the neck or the entire trunk may form the arc of a circle with convexity forwards. The rigidity of the neck is variable in intensity; it does not always appear at the beginning. It is increased when the patient assumes the sitting posture. The symptom persists even when the patient does not appear to suffer from pain in the spinal column.

This rigidity is not absolutely constant, and it is sometimes, especially in very young children, replaced by a sort of paralysis, in which the head may be moved in any direction without offering any resistance.

Contractures of the extremities are less frequently observed, but they occasionally occur, and we may even find *trismus* accompanied sometimes by dysphagia. Some patients suffer from convulsive rigid-

ity of the members, occurring in paroxysms and recalling that which is observed in tetanus.

Following the order of frequency of the symptoms, we have to mention *convulsions*, which are, however, much more rare than contractures. These convulsions may assume the aspect of epileptiform attacks, and may be limited to one side, presenting the characters of Jacksonian epilepsy. I have in one case observed convulsive paroxysms limited to one side of the face.

Paralysis is a much more uncommon symptom and in certain epidemics seems to be absent entirely, but ordinarily it is far from being an exceptional symptom. We not uncommonly note the existence of hemiplegia or of monoplegia, depending doubtless upon cortical lesions, or of paraplegia, due to spinal lesion. Paralysis of the eye muscles is much less frequent than it is in tuberculous meningitis, but still we cannot regard it as altogether exceptional. I have observed it in two of my cases, and it is mentioned by many authors. Corbin[28] noted it in two-thirds of his cases at Orleans, and Lewis Smith[162] found strabismus quite regularly.

Aphasia is not exceptional. I have observed it in one case, and Leyden has also mentioned its occurrence.

These paralyses occur sometimes suddenly, sometimes gradually. They may be purely temporary in character, as Forget[43] has shown, and this is especially the case in certain ocular paralyses. They may disappear gradually, and it is often absolutely impossible to foretell early what their future course may be.

Psychical Disturbances.—*Vertigo* figures among the initial phenomena. It is sometimes so severe as to make walking impossible, and some patients feel a whirling sensation which forces them to turn round and round, finally falling and being unable to rise.

Delirium is rarely absent. It is usually not very violent and is of a muttering character, though it may be exceedingly violent and accompanied by suicidal attempts. The patients may have hallucinations of sight and hearing. In some cases the delirium assumes the characters of some special form of mental alienation.

In a small number of cases the mental troubles persist indefinitely, even after recovery has taken place. Most frequently, however, their duration is brief, and the patient has frequent intervals of intelligence and consciousness even during the course of the disease. Faure Villars as early as 1839 insisted upon this peculiarity. "The delirium and coma yielded momentarily when the attention of the patient was fixed by a loud word. The replies were brief but lucid, and the preservation of the intelligence is not one of the least remarkable phenomena of the disease."

Insomnia is not constant.

Coma is a very frequent symptom in cerebrospinal meningitis. It may come on at the very beginning, being in fact the initial symptom, in which case it often persists up to the end, which is not long in coming. If the disease is prolonged the coma usually yields, but a return of consciousness is not a certain sign of a happy termination. The other symptoms may persist or increase, and in the last moments the coma may reappear.

Organs of Special Sense.—The symptoms referable to the *eyes* may be important. The pupils are often normal or they may be dilated, contracted, unequal, or sluggish in their reaction to light. Photophobia is a very common symptom. Sometimes patients complain of diplopia. Forget, Corbin, Hirsch, and others have noted the extreme frequency of conjunctivitis, characterized by congestion and deposits on the cornea. There may be keratitis and sometimes iritis, iridochoroiditis, and retinitis. Amblyopia and amaurosis have been noted several times. They are not necessarily permanent.

The *auditory apparatus* is much more frequently affected. Without speaking of tinnitus aurium, which is usually present in cerebrospinal meningitis, we often note deafness, either unilateral or bilateral, which may become permanent. As Forget, Lindström, and others have shown, this disease is a frequent cause of deaf-mutism. An examination of the drum membrane sometimes shows us the presence of an exudate in the tympanum which may result in perforation. The researches of Klebs and others have shown the frequency of suppurative inflammations of the tympanum, labyrinth, and semicircular canals. Lewis Smith found deafness persisting in about one-tenth of the cases that recovered.

The symptoms referable to the *olfactory apparatus* possess quite a considerable interest as regards their pathogenesis. We shall return to this at the proper time and here will say only that Ames was the first to note the loss of smell on one side, and that more recently Strümpell[164] has reported new facts of this nature.

Corbin[78] has reported one case of disturbances of the sense of taste.

The Skin.—The cutaneous symptoms are exceedingly important. Those which are most frequently observed are herpes, petechiæ, and lenticular rose spots.

Herpes may be a symptom of great value in cerebrospinal meningitis. It is ordinarily seated on the face and may differ in no respect from common labial herpes. Frequently, however, the herpetic eruption is much more abundant, occupying numerous areas, with confluent phlyctenoid vesicles scattered over the face and not confined to one side. These patches may also be observed upon the chest, the

shoulder (Jaffe[76]), and the hand. The eruption may appear as early as the second day, but comes more frequently on the fourth day. It rarely lasts beyond the eighth day. Tourdes believes that herpes is a symptom of good-omen, but most authors do not attribute to it any value in a prognostic sense. At Copenhagen the mortality in cases of meningitis accompanied by herpes was 35.2 per cent., while in those cases in which there was no eruption it was almost the same, namely, 35.5 per cent. In the course of the French epidemic of 1837–49, as also in the German epidemic, herpes was a quite frequent symptom. Tourdes found it in two-thirds of the cases, Leyden in three-quarters, Friis of Copenhagen noted it in half of his cases (54 out of 107), and Jaffe of Hamburg in 41 per cent. In the small epidemic which we have just passed through in Paris, herpes was remarkably rare. In Boston in 1897 it was reported in 35 out of 111 cases.

While in certain epidemics herpes constitutes the most constant and most characteristic eruption, in Ireland, Sweden, and America the usual exanthem of cerebrospinal meningitis has been of a *petechial* nature. It appears under the form of spots of various sizes, of an intense red or purple color, sometimes discrete, at other times confluent. These spots do not disappear under pressure of the finger. They persist without change for several days and then gradually fade. The petechial eruption is earlier in its appearance than herpes. It is of such common occurrence in America that it has given to the disease its popular name there of "spotted fever." A petechial eruption was also frequently observed at the beginning of this century in the epidemic recorded by Vieusseux and Mathey at Geneva. Although of rare occurrence in the epidemics in France and Germany, a petechial eruption has nevertheless been observed occasionally in them and has then seemed to indicate a more serious prognosis. In Copenhagen it was reported in only two cases, both terminating fatally. Githens observed it in forty-five out of ninety-eight cases. In Boston in 1897 it was noted in eleven out of one hundred and eleven cases. The petechiæ are especially well marked over the elbows and knees.

Lenticular rose spots, similar to those forming the exanthem of typhoid fever, have been occasionally noted, especially by Tourdes.

Among other eruptions which have been noted in cerebrospinal meningitis we find a scarlatiniform rash, urticaria, sudamina, and the lesions of ecthyma, but none of them occurs with such frequency as those above mentioned, nor does any of them possess equal significance. Furuncles have also been seen in the course of convalescence from cerebrospinal fever.

Temperature.—An elevated temperature is not a constant feature in epidemic cerebrospinal meningitis. Tourdes, from whom we quote

frequently, says on this point that the fever did not exist from the beginning; even in cases in which the pulse was accelerated the other elements composing what we rec-

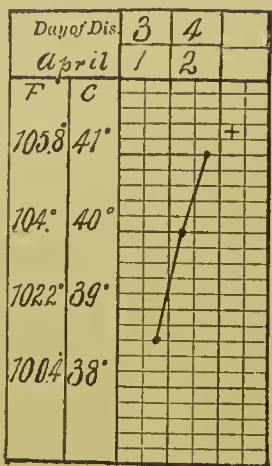

CHART No. 1.—Cerebrospinal Meningitis in a Child of two Years, Ending in Death.

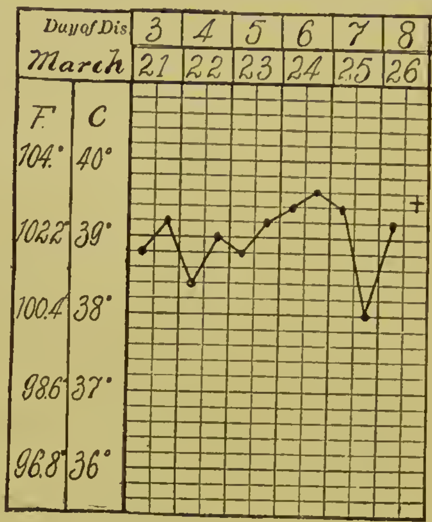

CHART No. 2.—Cerebrospinal Meningitis Ending in Death.

ognize as the febrile movement were not observed. The temperature of the skin remained natural, or sometimes was even reduced. The cases which terminated in death within the first few days ran an absolutely apyretic course, but when the affection was prolonged be-

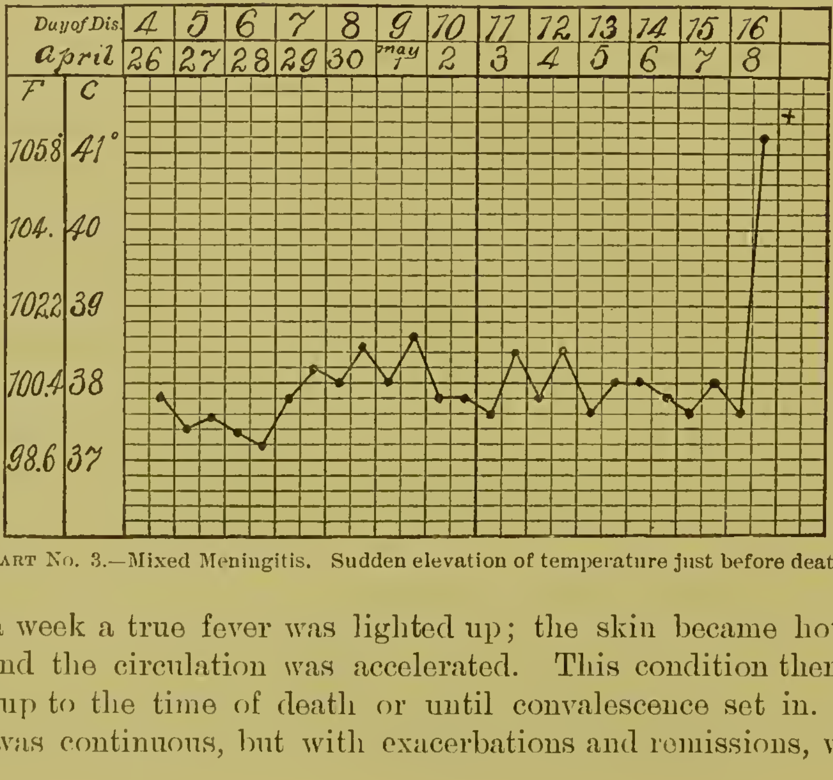

CHART No. 3.—Mixed Meningitis. Sudden elevation of temperature just before death.

yond a week a true fever was lighted up; the skin became hot and dry, and the circulation was accelerated. This condition then persisted up to the time of death or until convalescence set in. The fever was continuous, but with exacerbations and remissions, which

were sometimes so marked that the condition was believed to be one of genuine intermittent fever, and quinine was given with a lavish hand, but without effect. The rise in temperature occurred in the afternoon, but was not always of equal extent; it was usually accompanied by an exacerbation of the other grave symptoms. There was no regularity in the appearance of the chills and sweats.

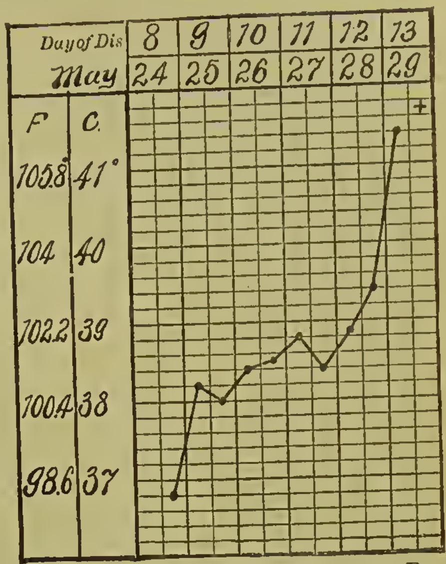

CHART No. 4.—Mixed Meningitis. Progressive elevation of temperature.

The use of the thermometer introduced by Wunderlich enabled clinicians to study more exactly and in greater detail the course of the fever, but repeated observations did not invalidate the statements of Tourdes. Cerebrospinal meningitis may be apyretic at the outset, and may remain so indefinitely. The fever may be absent in the fatal cases as well as in those which terminate favorably. Ordinarily, however, the temperature rises on the first or second day, and may reach 39° C. (102.2° F.), remaining then between this and 40° C. (104° F.), or even going as high as 40.5° or 41° C. (104.9° or 105.8° F.). In cases of short duration the temperature remains at this height without marked remission, but rises in case the termination is to be fatal (charts 1, 2, 3, and 4), and diminishing, ordinarily by lysis, in favorable cases (see charts 5, 6, and 8). In prolonged cases the temperature usually shows remissions which may follow the inverse type (see chart 7). Very often, when the disease lasts more than a month, there are periods of almost complete apyrexia interrupted by febrile paroxysms of short duration.

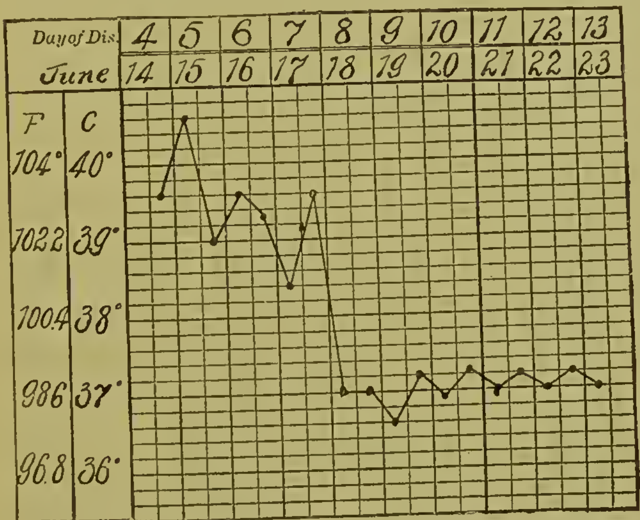

CHART No. 5.—Cerebrospinal Meningitis Ending in Recovery.

Pulse.—The condition of the circulation varies. At the beginning of the disease the pulse is ordinarily somewhat slow, and may be at

the same time irregular. This slow pulse does not last ordinarily more than three or four days and is then replaced by a notable acceleration. The pulse may be weak and irregular, but more often it is hard and small. Within the course of a few days it may present very opposite characteristics. Among its most remarkable characters is a great variation in frequency in very short periods of time. Thus within less than an hour Friis noted a pulse varying from 84 to 148 to the minute. In some cases terminating in recovery J. Lewis Smith, taking the pulse several times a day, obtained the following figures: Child of four months: 168, 120, 108, 120, 140, 150, 136, 128, 129; child of six

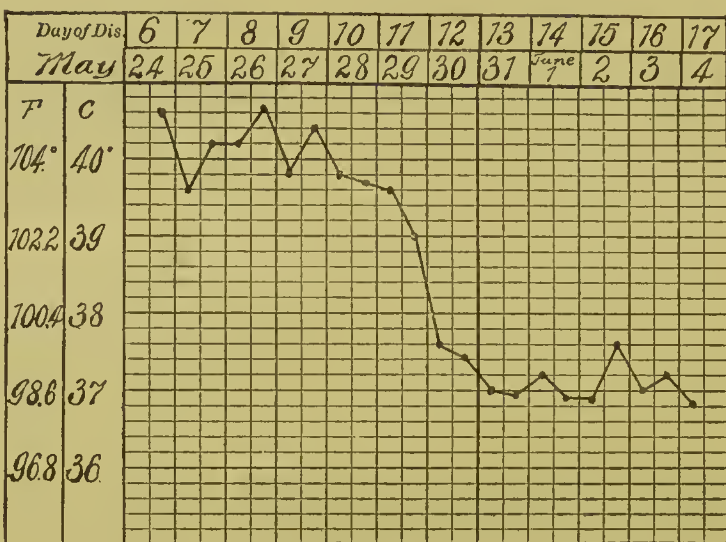

Chart No. 6.—Cerebrospinal Meningitis Ending in Recovery.

years: 120, 120, 88, 86, 92, 124, 128, 120. In a fatal case, in which the pulse was taken twice a day, he obtained the following figures: 204, 164, 116, 160, 164.

The *respiration* is often moaning, sighing, or interrupted, giving evidence of being labored even when the results of percussion and auscultation are negative. Sometimes we note a Cheyne-Stokes respiration, the appearance of which usually foretells a fatal issue. The average of thirty-one observations made by J. Lewis Smith showed a frequency of respiration of 42 to the minute.

Digestive Apparatus.—Nausea and *vomiting* almost always occur at the beginning of the disease, but cease later. The tongue is at first natural or covered with a white fur and later becomes yellow and rather dry.

Thirst is not marked. At the beginning the patient generally

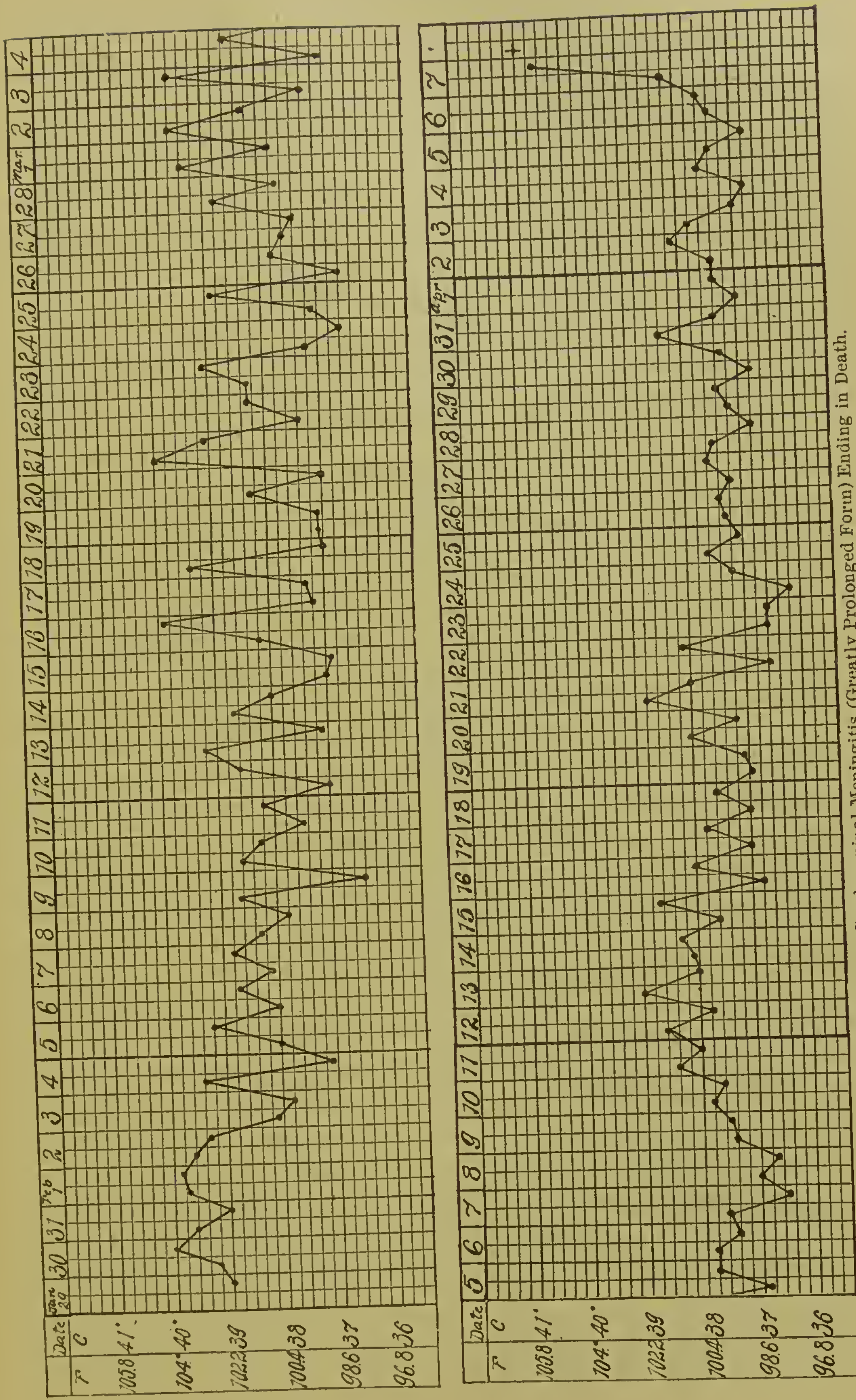

CHART No. 7.—Cerebrospinal Meningitis (Greatly Prolonged Form) Ending in Death.

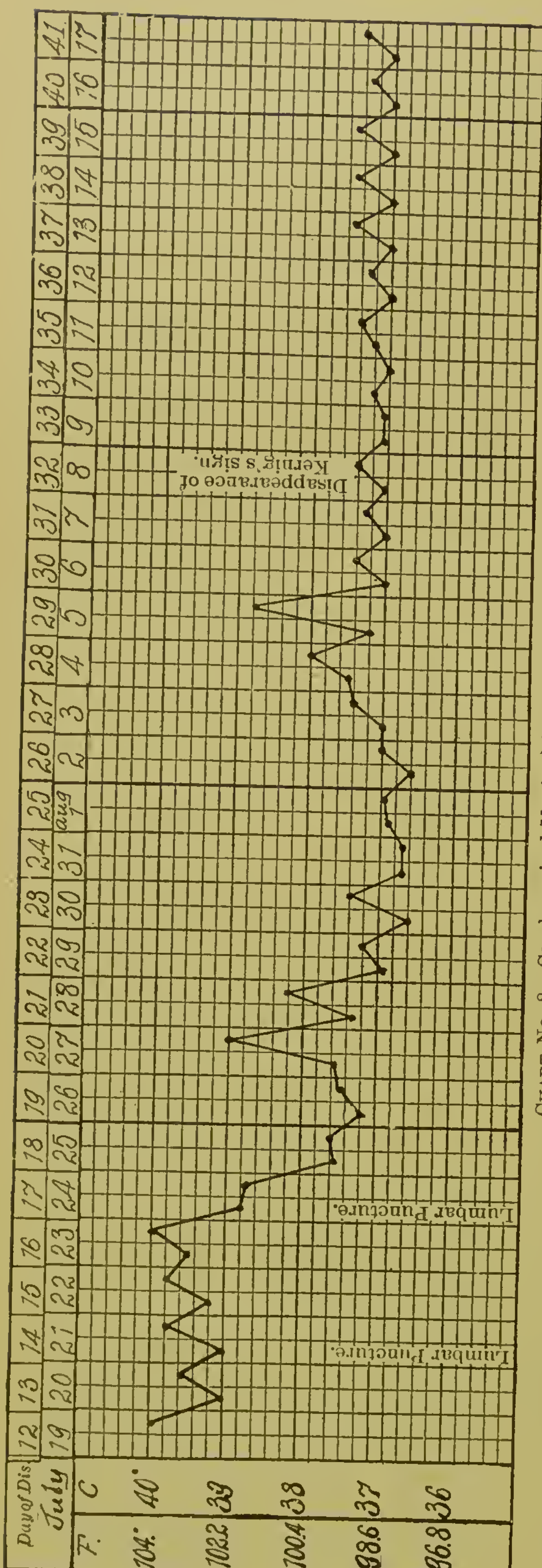

CHART No. 8.—Cerebrospinal Meningitis Ending in Recovery.

has *anorexia*, but it is usually possible to induce him to take food. Tourdes and most other writers say that the appetite usually returns early. During convalescence there is an insistent appetite which may even pass into boulimia.

Constipation is almost always present at the beginning, but rarely lasts more than a few days. It readily yields to mild laxatives, and the stools then become normal or diarrhœa sets in. The abdomen may at this time be normal in appearance, but ordinarily it is retracted as in cases of tuberculous meningitis.

The *spleen* in cerebrospinal meningitis usually presents but little change. Ziemssen found it enlarged in a small number of cases.

The *urine* is ordinarily passed in normal amount. It is pale and limpid. Sometimes during the acute stage there is polyuria (Ziemssen[181] and Mannkopf[103]). We find albumin in about one-third of the cases, but it is ordinarily scanty and purely febrile in its origin. In three out of ninety-seven cases Friis found albuminuria dependent upon acute nephritis, with tube casts and red blood globules in the urine. I have seen a similar case. Several writers have noted glycosuria.

Course, Duration, and Termination.

The *course* of cerebrospinal meningitis is quite variable. The disease may last from a few hours to thirty weeks.

In typical cases we may, with Faure Villars and Tourdes, distinguish three periods—namely, of invasion, reaction, and suppuration.

Period of Invasion.—In the first stage the organs are under the influence of the pathogenic agent and do not react against it. The functions of the nervous centres are profoundly disturbed and sometimes suddenly abolished; there is no fever, and no gastric phenomena except vomiting are noted. This period lasts from a few hours to three days, and the cutaneous eruption appears at its decline.

Period of Reaction.—The second period is marked first by a reaction of the organism, and we rarely fail to note a marked amelioration of the symptoms at its beginning. But soon the cerebrospinal phenomena regain their acute violence; their persistence indicates the occurrence of a purulent effusion. The pulse becomes rapid, gastric symptoms appear, and the fever which is at first inflammatory in character becomes typhoidal. This stage continues from the twenty-first to the twenty-eighth day on an average.

Stage of Suppuration.—In the third stage the functions of the nervous system are at once weakened and perverted. The patients no longer complain of pain, but rather of a general sensation of fatigue. They remain motionless with the body flexed, indifferent to all that goes on around them, the eyes are dull but prominent and covered with an albuminous film, which is thickest at the edge of the cornea. The tongue is cold and pale, sometimes dry, at other times moist. Deglutition is difficult. The digestive tract is very irritable, as shown by obstinate vomiting, hiccough, meteorism, and diarrhœa. The skin becomes dry. The extremities are cold. Eschars form over the sacrum, and the patient becomes deplorably weak and emaciated. In the closing days of the disease the pulse, which had been small, unequal, irregular, and slow, becomes frequent.

The *duration* of cerebrospinal meningitis in the epidemic at Strasburg (Tourdes) varied from nine hours to one hundred and nine days, the average being twenty days; the average duration of the fatal cases was fifteen days.

The *mortality* of cerebrospinal meningitis varies greatly in different epidemics. The following are some figures which we borrow from Hirsch:

Year.	Locality.	Cases.	Deaths.	Per cent.
1841	Aigues-Mortes	160	120	75
1838	Rochefort	153	107	70
1840	Strasburg	196	122	62.6
1839	Versailles	156	69	44.2
1841	Strasburg	230	90	40
1865	Rastadt	126	38	31.5
1856	Sweden	2,000	428	21.4

Hirsch has collected statistics embracing 15,632 cases with a mortality of 5,754, that is to say, 37 per cent. In Copenhagen the mortality was 48.8 per cent., in Boston[ix] it was 68.5 per cent. Leichtenstern of Cologne states that the mortality in the period from 1885 to 1892 was 19.2 per cent. Lewis Smith had 50 per cent. of recoveries in 1872, and 16 recoveries out of 35 cases after that date. In the recent epidemic at Paris, to which I have several times alluded, the mortality among my personal cases was 33 per cent., 7 out of 21 cases.

Death may occur very early in the course of the disease or it may take place at an advanced period, being then due to extreme exhaustion. The aspect of the patients in such cases shows very marked emaciation. Death may occur at any time from complications.

A certain number of cases terminate favorably within the first few days, the patient passing rapidly from a condition of extreme danger to complete health. Most frequently, however, the duration of the disease is longer, and recovery does not take place until after a long period of perilous convalescence.

Convalescence in cerebrospinal meningitis is long and difficult. The emaciation and debility are extreme. The headache recurs at intervals, and we may observe temporary delirium with hallucinations and fixed ideas, deafness, and a weakness or incomplete paralysis. The pulse is often accelerated. The appetite returns promptly and digestion seems to be easy, but the nutrition is poor and diarrhœa is common. Finally, after a longer or shorter period, with various ups and downs, the patient begins to take on flesh and his health becomes fully restored.

Recovery is usually complete without any *sequelæ*, although in some cases the neuralgias, paralyses, deafness, or amaurosis may become permanent. In young children we sometimes note the appearance of chronic hydrocephalus, characterized by paroxysms of cephalalgia with vomiting, loss of consciousness, convulsions, and involuntary passage of fæces and urine. These attacks recur regularly or irregularly, separated by intervals of sometimes several weeks' duration. During these remissions the patient's condition may be wholly satisfactory, the intelligence being preserved, the

special senses being normal, sleep calm, and appetite good. Usually, however, this period of calm is less complete, and we note the persistence of intellectual disturbances, of hyperæsthesia, or paralysis. The chronic hydrocephalus, which was noted by Tüngel[167] and Ziemssen,[181] is not very exceptional; it is susceptible of improvement or even of complete cure.

We may note cerebral or spinal palsies persisting after recovery from cerebrospinal meningitis. Various mental troubles may also be observed after recovery, but it is very rare to note permanent mental alienation as a sequel of this disease.

In view of both the gravity and the rarity of cerebrospinal meningitis, we may readily understand that *relapses* and second attacks are not common, nevertheless they have been observed. Boudin mentions the case of a corporal of the Sixty-ninth Regiment, who was in hospital four different times, from the 9th of January to the 24th of February, from the 3d to the 18th of May, from the 27th of May to the 9th of June, and from the 17th of June to the 20th, on which date he died. In the intervals of his hospital stay this man enjoyed apparently complete health, and was able to resume his military duties. It is probable, however, that in this case there was a prolonged meningitis with marked remissions, rather than true recurrence. In another case a soldier left the hospital cured in February, 1841, and reëntered the hospital in February, 1842, dying the day after admission. This was undoubtedly an instance of a second attack of the disease. In October, 1851, Boudin treated during a severe attack of cerebrospinal meningitis a soldier who had already suffered twice from the same disease in 1849 and a third time in 1850. We may also mention a case reported by North, in which a second attack occurred twenty-five months after the first, one of Hermann and Kober[64] at the end of a year, and another of Warschauer after five years.

Complications.

Epidemic cerebrospinal meningitis is, as we shall see, a general infectious disease whose most constant anatomical seat is the pia mater, but the effects of which are evident in all the organs. The predominance of one or the other of these aberrant localizations may become a source of complications. It is evident that the latter may be both very numerous and very diverse. A curious fact and one to which we shall have occasion to recur is that these complications vary according to the different epidemics. Thus, in certain epidemics the pleural or pulmonary complications occur with such frequency that the question arises whether there is not a very close

relationship between the pneumonia and the meningitis. This was especially marked in the American epidemics of 1807–16 and of 1873, and in the German epidemic of 1863–66. In other epidemics, as for instance that of Nauplia, reported by Kotsonopoulos,[87] inflammation of the joints occurred with remarkable frequency. In certain other epidemics complications on the part of the eyes or the ears have been very frequent. Even in the course of the same epidemic the complications may differ in their frequency and in their localization; thus pneumonia is often frequent at the beginning or end of the epidemic, but rare in the intervening period.

Let us study these complications in their anatomical order, apparatus by apparatus.

We will begin with complications on the part of the *organs of hearing and vision*. In the first authentic records which we have of cerebrospinal meningitis very little importance seems to have been attached to ear complications. Tourdes says that total deafness was always of very grave prognostic import, and he saw death occur in five cases in which this complication was present. He says also that deafness may persist for a considerable period during convalescence, and he compares this to the deafness frequently observed after typhoid fever. Moos[112] presents some very interesting figures as to the period at which these auditory troubles appear. In forty-three cases in which the date of the appearance of deafness was noted it came on twice during the first day, six times during the second, three times during the third, seventeen times during the period from the fourth to the tenth day, and fifteen times from the end of the first fortnight to the fourth month. Moos believes that quite a number of cases of deafness appearing in very young children are referable to an abortive attack of cerebrospinal meningitis. Voltolini,[170] on the other hand, believed that cerebrospinal meningitis was often confounded with inflammation of the labyrinth; most otologists, however, are not of his opinion and incline to accept the views enunciated by Moos.

The deafness may be permanent. Forget, Lindström, Wernicke, Knapp,[83] and Moos[42] have shown that when occurring in very young children cerebrospinal meningitis may be a cause of deaf-mutism, and they believe also that it is a not infrequent cause. The statistics cited by Ziemssen[180] bearing upon this point are very eloquent. At Nuremberg a count of the children in a school for deaf-mutes showed that twenty-two out of thirty-three children were thus afflicted in consequence of an attack of cerebrospinal meningitis, and in Bamberg this disease was responsible for the condition of every one of forty-two children who were inmates of a deaf-and-dumb asylum.

The auditory troubles are in most cases the result of inflamma-

tion and suppuration in the tympanum. These have been especially studied by Heller[61] and Klebs. In many cases the suppurative otitis results in a perforation of the drum membrane.

We have already noted the various alterations which the eyes may undergo. Loss of vision may follow optic neuritis, iridochoroiditis, keratitis, etc.

The complications on the part of the *respiratory apparatus* are of various kinds. We may note acute pneumonia, bronchopneumonia, bronchitis, pleurisy, and pulmonary gangrene. These complications vary in frequency in the different epidemics. Pneumonia was very commonly encountered in most of the epidemics in America, Sweden, Finland, and Germany, having then the characters of a frank acute pneumonia. We shall have occasion to return to this complication in the section on varieties, and especially in that on the pathogenesis of cerebrospinal meningitis. Alongside of these epidemics there have been others in which pneumonia was very rarely observed and in which the symptoms on the part of the lungs were insignificant and due chiefly to hypostasis.

Pericarditis and more rarely *endocarditis* have been noted in the course of certain epidemics.

We have already seen that epidemic cerebrospinal meningitis may be complicated by *nephritis*.

On the part of the *digestive apparatus* we may mention first certain cases of sore throat occurring sometimes at the beginning of an attack, persistent diarrhœa, and finally icterus which I have seen in one instance.

Not uncommonly subcutaneous *abscesses* and cases of suppurative parotiditis have been reported. Many writers have insisted particularly upon accidents of this sort, and have based upon their occurrence a theory that cerebrospinal meningitis is a suppurative fever or a form of pyæmia. This matter has, however, been definitely settled to the contrary by the results of bacteriological investigations.

Arthritis.—Articular pains are not at all rare in the course of cerebrospinal meningitis, and in a certain number of cases the joints are red and swollen, presenting all the signs of inflammation. The arthritis may in such cases be monoarticular (knee, shoulder, elbow, wrist) or involve at once a large number of articulations, resembling closely an attack of acute articular rheumatism. In most cases of this sort the inflammation terminates in resolution, even when there has been an effusion of considerable fluid in the affected joints. Many cases of this nature with favorable termination were reported by Tourdes as occurring during the epidemic at Strasburg. Even in cases in which an exploratory puncture has shown the purulent nature

of the effusion and the presence of the meningococcus has been proven (Fronz[50]) the inflammation may end in resolution. In certain cases, however, the disorders are more marked. There may occur peri-articular purulent collections, and ankylosis may result from the inflammation, even when arthrotomy has been practised early.

We would call special attention to the occurrence of arthropathies under the form of rheumatismal polyarthritis in the initial period of cerebrospinal meningitis. I have encountered cases of this kind, as has also Bäumler, and I am persuaded that they were not cases of rheumatism complicated with meningitis, but that they were cases of meningitis from the very beginning. Strümpell,[164] who has seen similar cases and who has also seen cases of rheumatism complicated with slightly marked meningitic phenomena, presents the problem without attempting to solve it. I believe that we can speak more positively to-day, thanks to the results of bacteriological research and thanks also to the early detection of Kernig's sign in cases of this nature.

The articular complications were relatively common in Paris during the small epidemic prevailing there the past year, and they were almost constant in the epidemic at Nauplia described by Kotsonopoulos.[87] In the German epidemics they were quite often encountered, but they were rarely met with in the French epidemics and seem to have been almost entirely wanting in most of the American and Irish epidemics. They were present, however, in about one-fourth of the cases reported by Flexner and Barker.[41] These articular complications are not confined exclusively to grave cases of cerebrospinal meningitis, but on the contrary in several epidemics their apparition seemed to be of favorable prognostic import.

Varieties.

We have already referred to the varied appearance which cerebrospinal meningitis may present. Most writers on the subject have thought themselves justified in distinguishing varieties of the disease which they made more or less numerous, their classifications being based upon the gravity of the disease, its duration, the seat of its lesions, and its symptoms. Tourdes divides the affection into eleven different forms, in the first seven of which the symptoms point to a lesion involving the entire cerebrospinal axis, and in the others the brain alone seemed to be affected. He saw no cases in which the symptoms made it probable that the disease was confined exclusively, or almost so, to the spinal cord. Other writers have, however, reported cases of this sort, and I have recently seen a child in whom

the symptoms seemed to indicate the existence of a simple acute spinal meningomyelitis.

The cerebrospinal forms in Tourdes' classification were the following: (1) Foudroyant; (2) convulsive comatose; (3) inflammatory; (4) typhoidal; (5) painful; (6) hectic; and (7) paralytic. The most common of these forms were the typhoidal, foudroyant, and painful. The cerebral forms of Tourdes were: (8) cephalalgic; (9) delirious cephalalgic; (10) delirious; and (11) comatose. The mortality was greater in the cerebrospinal forms (seventy-six per cent.) than in the cerebral (twenty-four per cent.). The foudroyant, comatose, convulsive, and hectic are the most dangerous of these varieties, and after them come the typhoid and inflammatory. The painful form is the least serious of all the cerebrospinal varieties, and there is no danger at all in the cephalalgic variety, which includes all the mild and doubtful forms of meningitis, even simple congestions occurring in the course of an epidemic of cerebrospinal meningitis.

Hirsch prefers a classification which takes less account of the symptoms than of the course of the disease and of its gravity. He distinguishes: I. The grave forms, which he subdivides into (1) foudroyant meningitis; (2) acute grave meningitis terminating in death or in a very gradual return to health; (3) grave meningitis with various complications, of long duration and ending in death in a typhoid state, from exhaustion or from some complication. II. Mild forms: (1) with characteristic but not severe symptoms, terminating ordinarily in recovery, except in cases in which a sudden and fatal exacerbation occurs; (2) with characteristic but very mild symptoms, fever being absent and the course of the disease being rapid. III. Extremely mild cases in which only a few of the symptoms appear—the abortive form. Hirsch distinguishes also continued, remittent, and intermittent varieties.

A third classification, no less interesting than the preceding, is that of Webber, who recognizes three principal varieties: I. In the first form very pronounced symptoms point to an alteration in the nervous centres—this is the classical meningitis. II. In the second form the most marked of the symptoms are referable to the lungs—this is the pneumonic variety. III. Finally in the third form the organs appear to be but slightly affected, the force of the disease seeming to be expended especially upon the blood and the integument.

I shall choose among each of these classifications the varieties which appear to me to deserve a special description; these are the foudroyant, abortive, typhoid, intermittent, pneumonic, cutaneous, and latent forms.

The *foudroyant form* of cerebrospinal meningitis strikes with a

brutal suddenness in the midst of apparent health, no prodromes having given warning of its approach. The child is seized in the midst of its games, the soldier while on guard or at drill, the laborer while at his ordinary occupation. The first symptom may be a chill or a dimness of vision, and almost instantaneously the patient falls into a state of coma; his face is pale or cyanotic and the pulse is small. This condition may continue unchanged till death or it may be interrupted by convulsions. Death may occur within six hours or it may be delayed for twelve, twenty-four, or thirty-six hours. These cases of foudroyant meningitis are especially frequent at the beginning of an epidemic and on this account their true nature is often not recognized, and according to circumstances we may be led to think of poisoning, insolation, a pernicious fever, or the like.

Abortive meningitis is characterized by the presence of some of the symptoms of cerebrospinal meningitis, but greatly attenuated and of short duration, terminating usually in a rapid return to health. These symptoms consist of headache, often of a periodic character and frequently accompanied by vertigo, a slight mental obfuscation, ringing in the ears, and a feeling of stiffness with some pain in the nucha and back. At other times the initial symptoms are more severe and consist in a violent chill, splitting headache, nausea and vomiting, quite marked ridigity of the nucha, insomnia, and nocturnal or even diurnal delirium. This state continues several days and terminates quite suddenly in a sort of crisis with profuse sweating or epistaxis (Hirsch). Sometimes convalescence is slow and stretches out over several weeks, the patients being weak and unable to pursue their usual occupations.

In some of my cases these abortive forms of meningitis were especially characterized by very violent pains in the extremities and might very readily have been confounded with influenza. The frequency of the abortive form of cerebrospinal meningitis varies in different epidemics. They are most often observed in children, and Kampf has remarked that they are especially common among the well-to-do classes.

It has been thought useful to describe an *intermittent variety* in which the symptoms present alternate exacerbations and remissions, variable both in their duration and in their periodicity. The intermissions may appear at the beginning of the attack, in its course, or at its decline; they are usually most marked in the evening, but all writers have mentioned particularly the frequency of the inverse type as apparent in the thermometric tracings. Clinicians have been misled by this intermittence to attribute the meningitis to the action of the malarial poison, and have consequently employed quinine in the

treatment, but the absolute inefficacy of this drug is proof sufficient that no relation whatever exists between meningitis and malaria.

It is proper to retain in this classification the *typhoid form*, in which the symptoms consist chiefly of mental confusion, stupor, and delirium. The tongue is dry and covered with a thick yellow fur, which is brown in the centre. There is meteorism and the stools are loose. When the eruption is, as is sometimes the case in meningitis, one of lenticular rose spots, the resemblance to typhoid fever is still more marked. We shall see how to avoid error when we come to discuss the diagnosis of epidemic cerebrospinal meningitis, and for the present we need only remark that the sudden onset of the disease and the coexistence of painful symptoms are little characteristic of enteric fever.

In certain American epidemics the nervous symptoms were less marked and the functional and physical signs of pneumonia assumed great prominence. This is the *pneumonic form* of Webber and of Smith. We shall have occasion to return to this variety in another part of this article. Similar cases have been observed at Stockholm by Medin.[106] They appear to be more common at the beginning of an epidemic than later.

In the *purpuric or petechial form* the cerebrospinal symptoms may be but little marked, even when the autopsy reveals the presence of evident organic lesions of the meninges. The most prominent symptoms are great physical depression and a petechial eruption. The symptomatic picture recalls that of typhus fever, and the differentiation is all the more difficult as epidemics of cerebrospinal meningitis have more than once coincided with those of typhus or relapsing fever. Such a coincidence has been observed in America and also in Europe at the end of the wars of the Empire. In Ireland in 1844 and again in 1866 cases of cerebrospinal meningitis presented at the beginning the type of purpuric fever in which death occurred during the first few hours, so as to excite in the observers of the early cases a suspicion of a return of the "black death" of the Middle Ages.[150] In this purpuric form the beginning is very violent. The patient complains of pain in the head, the back, and the extremities. The eruption may be confluent or discrete, and is petechial in character from the start. The ordinary symptoms of meningitis (stiffness of the nucha, paralyses, etc.) appear later or may be wanting, and this even in cases terminating in recovery.

In concluding this section we have yet to mention a modification in the appearance of the disease which the age of the patient may impose upon it. In very young children (Davidsohn[31]) an abnormal restlessness or somnolence may be the only symptoms present. Con-

siderable importance is attached to an examination of the fontanelles at this age, for they are apt to be very tense in cases of cerebrospinal meningitis. In the aged also suppurative cerebrospinal meningitis is apt to be latent (Inglessis[73]).

Diagnosis.

The diagnosis of epidemic cerebrospinal meningitis often presents great difficulties. The disease may be confounded with the most varied organic affections of the brain or of the spinal cord, with tuberculous meningitis, cerebral softening, brain tumors, myelitis, etc.; with the neuroses, hysteroepilepsy, tetanus, chorea; with general infectious diseases, such as typhus or typhoid fever, influenza, or pernicious malarial fever; with articular rheumatism, purpura, etc. I have personally seen instances in which each of the above-mentioned affections was simulated and some difficulty was experienced in differentiating between them and cerebrospinal meningitis. The operation of forming a diagnosis divides itself into two or more stages. We have first to determine whether meningitis is present, and then to decide whether it is epidemic cerebrospinal meningitis or some other form. The first question is one that is not always easy of solution, and indeed there are often very serious difficulties in the way. Unless one is always alive to the possibility of any given case being one of cerebrospinal meningitis, there is great danger that some isolated or very transitory symptom, which would give a clew to the diagnosis, may escape notice.

Between *typhoid fever* and cerebrospinal meningitis the differences are usually very well marked. The former begins insidiously, the latter noisily. The headache is generally much more severe in meningitis, and is accompanied by more or less rigidity of the nucha. The gastroenteric troubles are more pronounced in typhoid fever, and it is almost always possible to make out an enlargement of the spleen in this disease. The rose-colored eruption is the rule in typhoid fever, but is rare in meningitis. Nevertheless the resemblance between the two is sometimes very great, and just as we have seen that there is recognized a typhoidal form of meningitis, so there is a cerebrospinal form of typhoid fever. The two affections have been confounded more than once, the distinction not being made until the autopsy, and it may be necessary in certain cases to examine as to the agglutinative power of the serum or to determine the presence or absence of Kernig's sign before being assured of the correctness of our diagnosis.

Between *typhus fever* and the purpuric form of cerebrospinal menin-

gitis there would seem to be a greater chance of confusion, and all the more as in this form of meningitis the cerebral symptoms are often very rudimentary. In both diseases the onset is apt to be violent, in both there is purpura, in both the patient is delirious and has carphologia, muscular rigidity, and extreme prostration. Pneumonia, which is a frequent complication of meningitis, is likewise common in typhus fever. These close resemblances have led some very competent writers, and Murchison in particular, to deny that cerebrospinal meningitis has any individuality and to look upon it as simply a variety of typhus fever—an opinion which is shared by Webber.[ix] A fact which has tended greatly to increase the difficulty of a differential diagnosis in many cases is that epidemics of cerebrospinal meningitis have co-existed with those of typhus fever.

Boudin quotes the instructions addressed in January, 1814, on the occasion of an epidemic of typhus fever at Mayence, to all the prefects of the empire, from which we abstract here the following passages: "Le typhus s'annonce ordinairement par une pesanteur le long de l'épine, par des douleurs lombaires, des vomissements, une douleur de tête, des convulsions, des exacerbations régulières, du délire pendant la nuit, une déglutition difficile. A Mayence le typhus paraît souvent sous la forme d'une encéphalite avec mal de tête s'étendant du vertex à l'occiput et se prolongeant le long de la colonne épinière. Il y a état comateux ou délire feroce, dans quelques cas tétanos général. . . ." Boudin, who recognizes in this description the essential features of meningitis, is led by it to believe that typhus fever during the wars of the Empire was nothing more or less than cerebrospinal meningitis, thus following the same reasoning as Murchison, but in an inverse sense. The truth is, of course, that the two diseases are entirely distinct and should not be confounded, and the proof of this is the fact that the Irish physicians in 1866 were perfectly well able to distinguish the purpuric form of meningitis from typhus fever.

The chief elements in enabling us to arrive at a differential diagnosis are the suddenness of invasion, the almost immediate appearance in meningitis of the eruption, which in typhus fever does not become visible until the third or fourth day, the early appearance of delirium, which in typhus fever does not come on ordinarily until the end of the first week, the rigidity of the nucha in meningitis, and finally the much more contagious character of typhus fever.

Influenza in its nervous form presents certain symptoms which resemble very closely those of cerebrospinal meningitis. These are especially the pain in the head and back, the general soreness, and not infrequently delirium and vomiting. The onset in both cases is usually equally sudden. Influenza may even be accompanied with

suppurative lesions of the meninges, as Eugen Fränkel[45] observed in one case. But epidemics of cerebrospinal meningitis have sometimes coincided with those of influenza, and this adds a new difficulty to the diagnosis of the two affections. I am persuaded that the two have been confused a number of times, even in Paris, and that the cases of "grippal meningitis," upon the frequency of which several writers have remarked, were actually instances of epidemic cerebrospinal meningitis.

Kernig's Sign.—In order to determine with certainty the correct diagnosis in all such difficult cases we must look for a sign of great

A.

value, namely, Kernig's sign. This symptom, which was first brought to public attention in a Russian journal in 1882 and in a weekly paper of Berlin in 1884,[78] and the existence of which has been confirmed by Bull,[20] Henoch,[63] Blümm,[14] Friis,[48] and Netter,[128, 129] does not yet appear to be known as it deserves to be, and we may therefore profitably devote a few words to its consideration. When patients suffering from meningitis are placed in the dorsal decubitus, we do not ordinarily find any contractures of the lower extremities, the latter being readily flexed or extended in any direction by the hand of the examiner. But if we make the patients sit up we find that there is a certain degree of flexion of the knees, and on attempted extension we find that a slight contraction of the flexors prevents this movement

B.

C.

FIG. 4.—Illustrating Kernig's Sign. A, Cerebrospinal Meninigitis ; the child is lying down, an extension of the knee is made with ease. B, the same as A; the child is sitting, and full extension of the knee is impossible. C, Bronchiectasis; the child is sitting, but full extension of the knee is made with ease, showing the absence of Kernig's sign.

from being carried to its full extent. Usually the limb cannot be straightened beyond an angle of 135°, and sometimes not beyond a right angle. The contrast is most marked and absolute between the facility of extension of the knee when the patient is on his back and the invincible resistance when he is in the sitting posture.

Kernig found this sign present in fifteen cases of acute meningitis, in eight of which the diagnosis was confirmed at autopsy. In thirteen of the cases the disease was epidemic cerebrospinal meningitis, in one tuberculous meningitis, and in one suppurative meningitis complicating nephritis. Kernig says expressly that this sign is found only in cases of meningitis, and that he has never encountered it in cases in which the meninges were healthy. My personal investigations confirm absolutely those of the Russian physician, and I have been able to prove the existence of meningitis in forty-five patients in whom Kernig's sign was present. But, as Henoch [63] has remarked, Kernig's sign may be absent in meningitis, and I myself have seen five cases of meningitis in which it was wanting. In my cases the sign was present in forty-five cases out of fifty, that is to say in ninety per cent., and this is nearly the proportion found by Friis, who encountered it in fifty-three cases out of sixty. It may safely be said that in future an examination to determine the presence of Kernig's sign will be of necessity in all doubtful cases of meningitis. This has been of the greatest assistance to me in cases of doubt, and I have shown elsewhere that it enables one to make a diagnosis in the mild or abortive forms of meningitis. The symptom possesses one great advantage in that it can be elicited without the cooperation of the patient. As we have said, the sign is not encountered in any other affection than meningitis; it is absent even in tetanus, and Ombredanne[133a] has recently reported a case in which the absence of Kernig's sign enabled him to make the diagnosis of tetanus.

The mode of production of this sign is doubtless as follows: In consequence of the inflammation of the meninges the roots of the nerves become irritable, and the flexion of the thighs upon the pelvis when the patient is in the sitting posture elongates and consequently stretches the lumbar and sacral roots and thus increases their irritability. The attempt to extend the knee is insufficient to provoke a reflex contraction of the flexors while the patient lies on his back with the thighs extended upon the pelvis, but it does so when he assumes a sitting posture. This explanation of Kernig's sign leads to the assumption that it does not belong exclusively to epidemic cerebrospinal meningitis, but that it may be found as well in tuberculous meningitis and in those forms which are secondary to subacute or chronic inflammations. The only essential fact to its

production is that the meningitis be not confined to the cerebral meninges, but that it also involve, as it usually does, the spinal membranes.

The presence of Kernig's sign enables us in the great majority of cases to determine the first part of our diagnosis, namely, the existence of cerebrospinal meningitis. After that we have yet to determine its nature. This second step in the diagnosis, the establishment of the fact that the disease is really epidemic cerebrospinal meningitis, is sometimes one of very great difficulty.

It is especially with *tuberculous meningitis* that the disease is liable to be confounded, for the reason that the former is much the more common, and also because the symptoms of the two affections resemble each other closely. It is generally said, and with truth, that the onset of tuberculous meningitis is insidious and is accompanied by a lower temperature than is epidemic cerebrospinal meningitis, that the symptoms point more particularly to the presence of lesions at the base of the brain, and that it attacks by preference lymphatic subjects with personal or hereditary tuberculous antecedents; on the other hand, in cerebrospinal meningitis there is almost constantly rigidity of the nucha and of the back, and the disease is often marked by an eruption of herpes. But none of these elements has any absolute value, and herpes especially has been encountered quite frequently in tuberculous meningitis.

In many cases much information will be furnished by lumbar puncture, a procedure which we owe to Quincke. A trocar is introduced between the spinous processes and a certain amount of fluid is withdrawn from the lower cul-de-sac of the dura mater surrounding the cauda equina. Quincke advises that the puncture be made between the spinous processes of the third and fourth lumbar vertebræ. He places the patient on the side with the legs bent on the body and the spinal column flexed as far as possible. In the case of a child the puncture is made in the median line immediately above the spinous process, the trocar being introduced to a depth of two centimetres. In the adult, in order to avoid the thick ligaments, Quincke makes the puncture five to ten millimetres outside the median line at the level of the lower border of the spinous process. He introduces the trocar from above downwards in such a way as to puncture the dura mater in the median line. The instrument is introduced to a depth of from five to seven centimetres. I agree with Chipault in preferring a puncture made between the fifth lumbar and the first sacral vertebræ, and I prefer with Fürbringer to place the patient in a sitting posture inclined forwards.

The fluid so obtained may be readily examined in a variety of

ways—objective, chemical, microscopical, and microbiological. In many cases of cerebrospinal meningitis the liquid is cloudy and deposits a purulent sediment containing a large number of white cells and also microbes, both intra- and extracellular, which may be cultivated. The fluid also contains a fairly large proportion of albumin, from one to four parts per thousand. This method of examination is of great utility and is neither difficult nor dangerous to the patient, provided we observe the precaution of removing the fluid slowly and of taking away no more than the few cubic centimetres necessary for examination. We must not rely too confidently, however, upon the information furnished by lumbar puncture. Without speaking of the cases of dry puncture, we may obtain a perfectly clear and sterile fluid, especially if the meningitis has existed for several days. In such cases centrifugation will not give us a deposit sufficient for microscopical examination, and when culture experiments are undertaken we shall have to sow a great number of tubes and employ a great variety of culture media. Furthermore, we do not always find tubercle bacilli in cases of genuine tuberculous meningitis. The experience of different observers in this respect has been varied. Stadelmann obtained positive results in 3 out of 4 cases, König in 4 out of 5, Fürbringer in 7 out of 10.[29] On the other hand Lenharz found the bacilli in only 20 out of 46 cases, Cassel in 3 out of 9, Wilms in 1 out of 5, and Mya in 2 out of 15. Bernheim and Moser,[11] who have made most careful researches, tell us that even when the bacilli are present they are in very small number and consequently the search for them is long and tedious and we cannot look for rapid or accurate results from it. In 62 cases of tuberculous meningitis, in which lumbar puncture was made during life, no fluid was obtained in 2; the fluid contained no bacilli in 18; tubercle bacilli were present in very small number in 27, and were abundant in 15. My own statistics on this point are of no value, for the reason that while in some cases I have found the tubercle bacillus, in those cases in which I failed to find it my examination was not sufficiently prolonged to permit me to affirm its absence with absolute positiveness.

Finally the difficulty is greatly increased by the fact that in certain epidemics of cerebrospinal meningitis the cases of tuberculous meningitis are very numerous, and in such cases the cerebrospinal fluid may contain the agents of cerebrospinal meningitis. Holdheim[68] was the first to report a case of tuberculous meningitis in which the fluid withdrawn contained the meningococcus, but he attributed the finding to an accidental impurity. Heubner, Lenharz, and Netter have, however, observed similar cases in which there could be no question of contamination. This fact of the possibility of mixed

cerebrospinal meningitis is a most important one, and teaches us that in spite of apparently the best founded presumption we cannot always absolutely deny the tuberculous nature of any case of meningitis, and that the early hopes of the positive value of lumbar puncture are not fully justified.

A bacteriological examination may be made of other fluids of the body also. Bozzolo[17] obtained cultures of the pneumococcus from the blood in one case. I have also obtained positive results in four cases, finding in the blood not only this microbe, but also the diplococcus intracellularis, which some authors have asserted does not pass into the circulation. In order to obtain successful results we must employ rather large quantities of blood, say from one-quarter to one-half a cubic centimetre.

In certain exceptional cases I have been able to obtain positive results from an examination of the urine and of the sputum.

Scherer[167] and Jaeger have led us to hope for still more valuable results from an examination of the nasal mucus. This is easily obtained by means of a cotton swab introduced into the nostril. By microscopical examination and culture experiments Scherer was able to detect the diplococcus intracellularis in eighteen cases of cerebrospinal meningitis. In fifty other cases only two patients harbored the diplococcus; the first of these had been seized with a coryza after having disinfected a room in which a patient with meningitis had been ill, and the second had been treated for a typhoid fever, complicated by ocular paralysis, and which may very possibly have been a case of meningitis. Presented in this way, the facts of Scherer seem to be quite demonstrative, but I do not think we ought to accept them without reserve, for personally I have obtained no satisfactory results from the examination of the nasal mucus. I may recall the fact that we almost always find in the nasal mucus, even in health, the pneumococcus, which is one of the agents of meningitis[120]; and Heubner and his pupil Slavyk have observed the same fact in relation to the diplococcus intracellularis.

Still another question is whether the cerebrospinal meningitis is an epidemic meningitis. The solution of this question is exceedingly difficult in cases occurring at the beginning of an epidemic, and even in the course of certain epidemics which, as we shall see, are remarkable by reason of the relatively small number of cases and by the absence of any appreciable relation between them. We shall see in a later section what the doctrine is concerning the relation of sporadic to epidemic meningitis, and we shall see that cases of primary meningitis which are apparently sporadic, tuberculous meningitis being excluded, are of the same nature as epidemic meningitis. As regards

cases of secondary meningitis a careful examination of the patient will enable us to determine whether they are due to insolation, to traumatism, to erysipelas, to otitis, or to a pneumonia, and we shall in this way be able to determine their nature. We shall show that certain cases of secondary meningitis, apparently wholly independent of epidemic cerebrospinal meningitis, are, however, related to the latter, and this is especially so in many cases which follow pneumonia, otitis, or even a cranial injury or a brain tumor.

Prognosis.

Cerebrospinal meningitis is a very serious affection, often terminating in death or leaving behind it incurable affections, such as paralysis, complete deafness, etc. It is far, however, from being always fatal and in this respect contrasts favorably with tuberculous meningitis.

It has been said above that the mortality varies in the different epidemics from thirty to seventy-five per cent. of the cases, and that, as a general rule, the gravity is less towards the end of an epidemic. In the epidemic at Strasburg, so carefully studied by Tourdes, the gravest cases were seen at the beginning and at the end of the epidemic. The following are the statistics of the epidemic as it occurred in the garrison there:

Date.	Cases.	Deaths.	Per cent.
1840, October	1	1	100
November	3	3	100
December	8	8	100
1841, January	34	23	67.64
February	43	32	74.41
March	65	36	55.38
April	29	10	34.48
May	9	6	66.66
June	4	3	75

In the epidemic at Versailles, studied by Faure Villars, the following figures were reported:

Date.	Cases.	Deaths.	Per cent.
1841, February	72	26	36.1
March	28	11	39.3
April	17	8	47
May	27	20	74
June	11	5	45
July	1	0	0

In the epidemic at Copenhagen, described by Friis, the mortality was as follows:

Date.	Cases.	Deaths.	Per cent.
1885, December	4	1	25
1886, January	2	0	0
February	7	4	57
March	17	7	41
April	35	13	37
May	21	9	43
June	15	5	33
July	3	0	0
August	5	2	40
November	1	0	0
December	3	3	100

The mortality is greatest in very young children, and is least among adolescents. The following are the figures given by Friis:

Age.	Cases.	Deaths.	Per cent.
Below 1 year	18	14	77.7
From 1 to 5 years	39	19	48.7
" 5 " 10 "	31	16	51.6
" 10 " 15 "	14	4	21.4
" 15 " 20 "	17	6	35.3
" 20 " 30 "	28	12	42.9
" 30 " 40 "	11	6	54.6
" 40 " 50 "	7	2	28.6
Over 50 years	5	4	80.0

The mortality figures are a little higher in females.

The prognosis naturally varies according to the form of the disease and with the number and violence of the symptoms. Convulsions, coma, marked changes in rhythm of the pulse and of the respiration are of evil prognostic import. The occurrence of herpes has no prognostic value.

It must not be forgotten that in the course of cerebrospinal meningitis remissions often occur, and we must not in such cases assume too hastily that recovery is about to ensue.

Treatment.

Bloodletting, narcotics, calomel, blisters, applications of ice, and quinine have all been proposed in the treatment of cerebrospinal meningitis, and each of them has its advocates and its adversaries.

Bloodletting was naturally frequently employed at the time when cerebrospinal meningitis first appeared in France, because at that period the antiphlogistic method of treatment was at its apogee.

Faure Villars claimed to have obtained very satisfactory results, and he believed that when phlebotomy was resorted to at the beginning of the disease it would abort it. But in order to obtain this result it was necessary, he held, to abstract a large quantity of blood, even to the point of inducing syncope. In addition to the phlebotomy the physicians of that time resorted to wet-cupping and the application of leeches to the temples, back of the neck, and along the spine. The antiphlogistic method, however, did not fulfil its early promises, and Tourdes already betrayed considerable scepticism concerning its advisability. At the present day, of course, it is wholly abandoned.

Opium was advocated especially by Chauffard[23] of Avignon, who claimed to have had wonderful results from its use. He prescribed it from the very beginning of the attack, employing it in large doses, reaching even 0.3 or 0.4 gm. (gr. ivss.–vi.) a day. By means of this remedy he claims to have saved at least fifty per cent. of his grave cases, and to have calmed those patients whom he could not cure. Since Chauffard's time opium is no longer regarded as a specific, but it is often resorted to in the shape of Dover's powder, and especially of morphine, in cases in which pain is very severe or the symptoms of mental excitement are prominent. We shall see, however, that we have at the present day other measures which are equally efficacious in the overcoming of these symptoms.

Lewis Smith reports excellent results from the use of bromide of potassium in large doses. Calomel was abandoned long ago, and vesication is also no longer resorted to. Iodide of potassium which is employed empirically in cases of meningeal inflammation and which is credited with some cures in the case of tuberculous meningitis has been prescribed very frequently in cerebrospinal meningitis, without, however, having proved its utility.

The application of ice bags to the head and along the spinal column usually quiets the pain and is to be recommended.

Such were, up to within the past four years, the measures employed in the treatment of epidemic cerebrospinal meningitis.

We owe to Aufrecht,[5] of Magdeburg, the introduction of a new method of treatment, the value of which has been definitely proven. This consists in warm bathing. In his first communication in 1894, Aufrecht was able to report but one case cured in which he had employed warm baths (one a day). The following year Voroshilsky,[187] of Odessa, reported two new cases in which he had employed baths of ten minutes' duration at a temperature of 40° C. (104° F.), given three times a day. Borling and Kellmeyer of St. Petersburg, and Steckel of Vienna, have also used these baths with good effect. I employed the same method in six cases (in all of which recovery

ensued), giving the baths in the case of children at least every three hours. The immediate effect of these baths upon the pain and the rigidity is very marked—so great, indeed, that the patients often call for a repetition. The muscular contraction becomes less marked, the pulse less frequent and more regular, and the temperature falls. We may profit by this improvement by giving the patient while he is still in the bath some bouillon or milk. My personal experience has led me to regard the warm bath as a specific method of treatment of cerebrospinal meningitis. In cases of moderate intensity three baths a day may be given, and to children, at least in the more severe cases, we may give a bath every three or four hours.

In conjunction with warm baths I prescribe salicylic acid or salicylate of sodium, which seems to be indicated as an antipyretic and analgesic. I have also used with advantage local applications of salicylate of methyl. Czoniker[30] has also obtained good results from the use of the salicylate.

Naturally we must endeavor to maintain the patient's strength by a mild diet of bouillon and milk, to which may be added, when the fever subsides, eggs, etc. I have remarked, with most writers on this subject, that there is less difficulty in alimentation in cases of meningitis than in other affections. With a little insistence the patient is quite easily aroused from semi-torpor or delirium and can be made to take nourishment.

In cases of extreme cardiac weakness we must resort to injections of camphorated oil, of caffeine, or even of strychnine, but the latter must not be given for such a time or in such doses as to increase the muscular contractions.

We have spoken above of lumbar puncture and its utility as regards diagnosis. It has also been recommended in the treatment of cerebrospinal meningitis, and its employment is justified by the fact that by it we may relieve intraventricular pressure and so remove a cause of some of the most troublesome symptoms. Some authors claim that this procedure gives satisfactory results in cases of meningitis; I myself have seen convulsions which had lasted without interruption for a long time cease after the withdrawal of only about two drachms of fluid, and others have noted a return of consciousness after lumbar puncture. I cannot, however, advise the employment of this puncture as a curative measure. We cannot always accomplish by it all that we hope for, as it has been shown that there is not always free communication between the lumbar cul-de-sac and the cerebral ventricles; furthermore, the withdrawal of too great a quantity of cerebrospinal fluid may cause a sudden removal of pressure which may provoke very grave symptoms or even cause death. This

opinion is not held by me alone, and, indeed, at the present time lumbar puncture as a curative measure in acute cerebrospinal meningitis is regarded as scarcely justifiable.

Bela Angyan[4] says that he has obtained very satisfactory results from hypodermic injections of corrosive sublimate along the spinal column. Of thirty patients treated in this way twenty-one recovered, a percentage of seventy. He employs the sublimate in aqueous solution in daily doses of one centigram for adults and half a centigram for children and continues this medication until the rigidity has disappeared. In his cases he gave at various times from four to twenty-four injections. I have had no personal experience with this method, but I have used mercurial frictions as also iodoform frictions, and I cannot say that the results so obtained were at all comparable to those of the warm bath.

Webber tells us that in America ergot, permanganate of potassium, and sulphite of sodium have been employed with success. Out of five cases treated with ergot there were four recoveries. This same remedy has also been recommended by Leyden, and Smith regards it as of decided utility. Munroe and Pearce have also had successful results from the employment of sulphite of sodium.

Isaac Kay obtained a cure in three cases out of four in which he gave permanganate of potassium, a tablespoonful every hour of a solution of one grain to the ounce. I have not employed this remedy, although its use would appear to be rational. We know, indeed, from the experience of Moor, of New York, that permanganate of potassium is a specific remedy for morphine poisoning. It doubtless acts by oxidizing. I have employed it with good results in certain cases of autointoxication, and it is very possible it would equally modify the poison elaborated by the pathogenic agent of meningitis.

During convalescence and in prolonged cases of the disease the medication should be especially tonic and supporting.

Pathological Anatomy.

The cerebrospinal axis is the seat of the chief lesions in cerebrospinal meningitis. Anatomically the disease is characterized by a purulent effusion on the surface of the nervous centres.

The integuments of the cranium and the dura mater present no special change. The sinuses of the latter are almost always filled with very dense blood clots.

The parietal layer of the arachnoid is not changed, but the visceral layer rests upon the purulent effusion. We distinguish beneath the serous membrane the yellow layer covering the pia mater, but the

arachnoid is not adherent to the false membrane which it covers; it is detached quite readily from the brain and cord, a simple inflation serving to raise it in its entirety. As a rule the arachnoid, notwithstanding its contact with the pus, preserves its transparency and remains evidently healthy even when it covers very extensive purulent exudations. Sometimes, however, it is whitish and opaque over the cerebellum and at other points. This opacity is seen often in old cases and indicates a process of absorption. The cavity of the arachnoid usually contains a small amount of serous fluid in which I have sometimes observed purulent flocculi, an observation made also by Tourdes.

The pia mater is the seat of the characteristic lesions. The exudation upon its surface presents different aspects; sometimes it is a yellowish diffluent liquid, sometimes a thick pus, and more often a dense yellowish false membrane of a thickness varying from three to six millimetres, resembling a layer of butter spread over the surface of the brain. When the effusion is scanty, it is distributed in the form of more or less wide yellow streaks along the course of the great veins of the brain, over the scissuras, in the interval separating the convolutions, and along the tortuous veins of the posterior portions of the cord. At other times the pus is disseminated in patches of variable dimensions, the brain being covered with purulent islets, more or less close to each other, the diameter of which varies from one to several centimetres. Finally, the false membrane may be of very considerable extent and may then look like a new meningeal layer. The pus often remains on the surface of the pia mater and is more or less adherent to it, but does not penetrate between the convolutions. At other times it descends to the very bottom of the sulci.

The physical properties of the pus vary according to the period of the disease. It is fluid at the beginning, but strikes us by reason of its viscosity, which is due, according to Klebs, to the presence of mucin; it soon, however, becomes more or less consistent, and it may even be converted into a false membrane of considerable toughness.

The pia mater is greatly congested, its smaller vessels are filled with blood, while the larger veins contain firm clots. In some cases, however, especially when the exudate is thick, the membrane is remarkably pale. The serous fluid contained in its meshes is generally abundant and limpid, notwithstanding the presence of the pseudomembranous layer, but sometimes it is cloudy and purulent. In some cases of rapid development in which the false membranes have not had time to form I have found an amber-colored fluid. The spinal fluid is always milky and mixed with pus, even when the false membrane does not extend to the cord.

Over the brain the false membranes cover both the convexity and the base, but more frequently the former. According to the case the lesions are more marked on one or the other hemisphere and in the anterior or posterior region. Sometimes, but not always, the symptoms bear an evident relation to the predominant localizations of the disease.

The cerebellum is almost always covered by a false membrane.

In the spinal cord the lesions are most marked in the lower portions. As a rule the false membranes are more numerous on the posterior surface, which not infrequently is the only part affected, this localization being the result of the decubitus and presenting nothing specific. In one case, however, I have found the false membrane limited to the anterior surface, and Tourdes reports a similar case.

The brain and spinal cord are the seat of some macroscopic lesions, such as congestion, centres of capillary apoplexy, and diffuse or circumscribed softening. In a certain number of cases we find abscesses. Strümpell has seen three cases in which a cerebral abscess coincided with meningitis and one case of cerebral abscess without meningitis. Such cases are not isolated.

The participation of the brain and cord is made still more evident by microscopical examination. Klebs has noted the presence of a diffuse encephalitis, and Flexner and Barker have found in the brain and cord collections of white cells surrounding the vessels like miniature tubercles. The vessels are dilated. Changes of a like nature are found at the level of the nerve roots, and Councilman has studied similar lesions in the Gasserian ganglion.

Voroshinsky and Leichtenstern have noted an extension of the exudate along the spinal nerve roots, and I have myself more than once noted the presence of purulent collections within the spinal canal, outside of the dura mater, which were due to a similar extension.

The purulent exudation may be produced in a very short time. Tourdes found it in the case of a soldier who died twenty hours after the beginning of the disease, and Gordon has reported a case in which the purulent exudate existed five hours after the beginning of the attack. In cases in which death occurs very rapidly, and doubtless also in those in which recovery occurs within a few days, there may be no exudation, the only thing found then being congestion of the pia mater with an effusion of clear or amber-colored serum. Tourdes found in two cases marked dryness of the membranes, and the microscope in these cases showed to Klebs a marked preponderance of cellular lesions. These lesions do not differ from those observed in simple meningitis. Councilman believes that microscopical examination will reveal to us an element of differentiation, the lining mem-

brane of the arteries presenting no change in epidemic cerebrospinal meningitis, while it is inflamed and proliferating in other varieties of meningitis.

Heller has described with much care the changes in the auditory apparatus occurring in cerebrospinal meningitis. He found on both sides a yellow, cloudy, purulent fluid in the tympanum, the vestibules, and the semicircular canals. The facial and auditory nerves were bathed in the pus. These changes are common. They may be limited to the middle ear or to the internal ear, but most frequently involve both. Certain writers, especially Heller, believe that these changes are due to a propagation of the inflammation along the nerves. Moos[112] believes that the changes in the internal ear and in the meninges occur simultaneously, the pathogenic agents acting on both at the same time. In a certain number of cases, however, the lesion of the ear is the primary manifestation, and we are then justified in regarding the meningitis as due to extension of the inflammation. Leyden, Baginsky, Leichtenstern, and others have reported cases in which acute otitis preceded the meningitis by several days.

The lesions in meningitis are not limited to the nervous centres and the nerves. There is an appreciable alteration of the blood. At a time when bloodletting was common it was found that the blood contained a considerable amount of fibrin. Recent hæmatoscopic investigations have shown that there is a very appreciable degree of leucocytosis in meningitis. Halla and v. Limbeck were the first to note this leucocytosis, and Rieder found in one case 20,100 and in another case 17,500 white blood cells to the cubic millimetre. Flexner and Barker have made these researches in a much greater number of cases, and they always found a very notable increase, the number of white blood cells varying from 12,000 to 32,000 per cubic millimetre. This increase was chiefly of the polynuclear and neutrophile cells, the proportion of eosinophile cells not being changed. This leucocytosis has also been noted in the Boston epidemic. It recalls the increase in the number of white cells observed in cases of acute pneumonia. Flexner and Barker noted that this hyperleucocytosis is encountered in fatal cases of meningitis as well as in those ending in recovery, so that we cannot attribute to it a prognostic value, such as it has in pneumonia. This probably finds its explanation in the fact that death in meningitis is due less to the infection itself than to the organic changes in the nerve centres.

In the intestines we often find Peyer's patches more distinct, but they are not projecting and are never ulcerated. The shaven-chin appearance is evident. The solitary follicles are more conspicuous and whitish.

The respiratory organs are more or less frequently affected according to the epidemic. Lesions of these organs were rare in the French epidemics from 1837 to 1848, but we frequently find mention of pneumonia in America and in Germany. These pneumonias were croupous or catarrhal in character. During the late epidemics in Stuttgart, Vienna, and Boston (1896), mention is frequently made of peculiar pulmonary lesions consisting of minute nodular foci, from the size of a pea to that of a filbert, of a brownish or reddish color, in which the pathogenic agents of the meningitis were found.

On the part of the circulatory apparatus we find mention of fibrinopurulent or purulent pericarditis, of ulcerative endocarditis, the frequent association of which with pneumonia and meningitis has been pointed out by Heschl and Netter.

The joints may be the seat of lesions of varying intensity, sometimes of a suppurative character. Finally, we have to note phlegmons of the cellular tissue which have been described in various parts of the body.

The following lesions, a description of which we borrow from Klebs, possess no specific characters, but are similar to those encountered in other infectious diseases of some duration, and especially in typhoid fever. Klebs found the spleen small and flaccid, the pulp being of a dark-red color, the follicles sometimes but slightly prominent, sometimes enlarged. In cases in which death occurred early in the course of the disease the spleen was found increased in size.

The kidneys are softer than normal, the capsule is easily separated, the surface is smooth and of a grayish tint. On section the medullary substance is found markedly congested, while the cortex shows alternate areas of red and grayish hue. The epithelium of the convoluted tubes has undergone granular degeneration.

The liver is rarely increased in size; it is less firm than normal, and on section is seen to be of a yellowish-gray color and dry, as if it had been boiled. Its cellular elements show evidences of a degeneration similar to that noted in the renal epithelium.

The muscular tissue is in part granulofatty degenerated. The voluntary muscles are flaccid and of a brownish-red color. The cardiac muscle is affected in the same way as are the other muscles, but fatty degeneration is never very marked.

Bacteriology.

Epidemic cerebrospinal meningitis is a microbic disease, the pathogenic agents of which are found in greater or less abundance in the exudate. We shall devote considerable space to this part of our study, as from many points of view it is of great importance.

History.

We shall mention here only those investigations which have had for their object primary meningitis, leaving aside those dealing with the secondary affection. Klebs[80] regards meningitis as due to the action of a monad, which he regards as the same as that of pneumonia, the monas pulmonale. Eberth,[35] in a case of suppurative meningitis complicating pneumonia, found corpuscles varying in shape from slightly ovoid to round. These corpuscles were sometimes solitary, but usually joined. They were readily stained by methylene blue.

In 1881 Aufrecht[6] noted the presence of micrococci in the meninges. These microbes were found outside of and within the cells, and they were also found in the blood, the spleen, and the lungs.

Brigidi and Banti[18] found in the pia mater rod-like bodies arranged in chains. They did not obtain cultures from these, but a guinea-pig, which had received an injection of them into the peritoneum, succumbed to peritonitis the following day. Gaucher[52] also described, in 1881, micrococci which he found in the meningeal exudate, the blood, and the urine.

These early publications lack precision, which is very natural, considering the primitive nature of the methods of investigation at this time. The following works, however, are of greater value.

On February 19th, 1883, Leyden[97] announced in a paper read before the Medical Society of Berlin that he had found in a case of cerebro-spinal meningitis occurring after double otitis certain oval-shaped microbes joined in twos or in larger groups. These microbes bore a striking resemblance to those of pneumonia and of erysipelas, but he thought that they differed from them by their greater size and more distinctly oval shape. Leyden did not attempt to obtain cultures of these microorganisms.

Marchiafava and Celli[103a] in 1884 described the presence of free or intracellular cocci in the pus of meningitis. They did not find them, however, in the blood or in the organs.

Leichtenstern in 1885 obtained from the purulent exudate micrococci taking aniline stains. These microbes occurred singly or as diplococci, and were free or enclosed in the cells. They were sometimes found in very small quantity. Leichtenstern was unable at that time to cultivate the microbes, although he tried various media.

Silverskjold and Almquist found a small bacillus or diplococcus which they were unable to cultivate. In Copenhagen in 1886 Rovsing and Christmas Dirkink Holmfeld found in two cases diplococci of

an elongated, oval form, contained within the cells; some cells having as many as twenty. The first attempts to cultivate these microbes were negative in their results, but later Rovsing obtained cultures on gelatin of an ovoid bacillus, non-pathogenic in character.

Early in 1886 appeared almost simultaneously communications by Netter,[117] Fraenkel,[44] and Foà and Uffreduzzi,[42] and these were followed by one of Guiffrey. All these investigators found in cases of

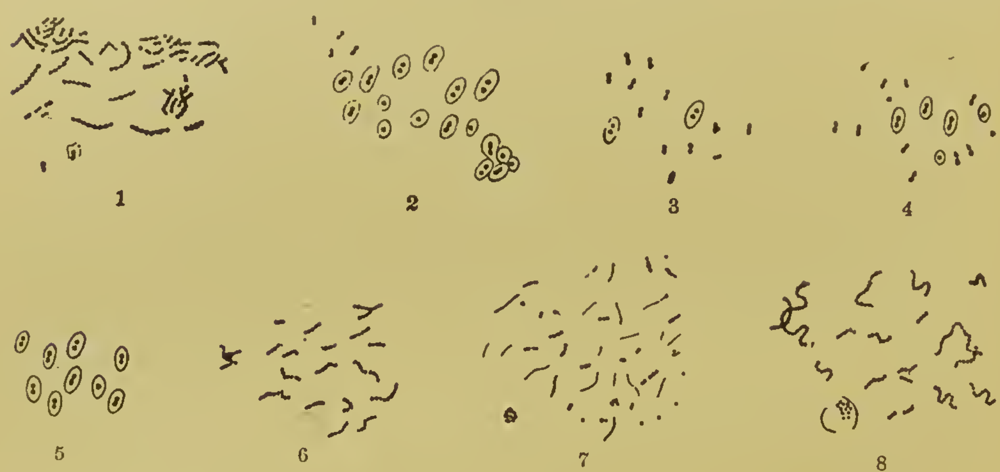

FIG. 5.—1, Lanceolate Pneumococci, arranged in linear series, from a case of meningitis secondary to pneumonia (found in the perivascular sheath); 2, encapsulated pneumococci, from a case of primary sporadic cerebrospinal meningitis; 3, encapsulated pneumococci, from a case of purulent otitis occurring in the course of an acute pneumonia; 4, encapsulated pneumococci, from a case of meningitis occurring in the course of typhoid fever, not complicated by pneumonia; 5, pneumococci, from a case of cerebrospinal meningitis coinciding with ulcerative endocarditis, not complicated by pneumonia; 6, streptococci, from a case of suppurative meningitis secondary to a suppurative pneumonia; 7, very delicate curved bacilli and micrococci, from a case of primary sporadic cerebrospinal meningitis; 8, streptococci, from a case of suppurative meningitis following caries of the petrous portion of the temporal bone. These figures represent the appearance of the microbes observed with ocular No. 1 and objective No. 12 (homogeneous immersion lens) of Verick. (Netter, 1887.)

primary suppurative meningitis, independent of pneumonia, an encapsulated coccus disposed in twos or in chains, which could be cultivated and the pathogenic action of which they studied in animals. This microbe presented characters identical with those of the pneumococcus. As early as 1884 and 1885 the present writer[116] had seen and described the same microbe in cases of primary meningitis accompanied by ulcerative endocarditis, but he was unable at that time to obtain pure cultures. The cases of meningitis in Paris and Berlin were isolated or few in number, and it might be questioned whether they were really instances of epidemic meningitis, but in the cases observed by Foà and Uffreduzzi at Turin no such doubt existed, for the investigations were made during the existence of an epidemic in March, 1886; and the same certainty existed in cases observed by Lemoine[94] at Orleans, where there were fourteen cases, with seven

deaths, of cerebrospinal meningitis between February and May, 1886, in two regiments of the garrison. In pus collected from these cases Widal found the micrococcus lanceolatus capsulatus, and he gave me the opportunity to confirm his observations. The character of epidemic meningitis was very evident also in the cases reported by Oebecke[133] at Bonn in 1886. They were of two brothers simultaneously attacked. In pus collected from these two cases Ribbert found cocci disposed in chains which developed on agar only at the temperature of the human body. He was unable to obtain fresh cultures by transplanting these some days later to a new medium. This short life is, as we know, one of the characteristics of the pneumococcus.

At the same time that the pneumococcus was found in these cases of sporadic or epidemic meningitis, uncomplicated by pneumonia, it was found also by many investigators in the exudate in cases of suppurative meningitis secondary to pneumonia. These cases of meningitis occurred with unusual frequency in 1886, a year which was marked almost universally by the number and gravity of pneumonias encountered. The pneumococcus was found very frequently in cases of meningitis in 1887 and subsequent years, especially by Weichselbaum,[173] Ortmann,[134] Hauser, Monti,[109] Banti,[8] Mirto,[107] Klippel,[84] and Flexner and Barker.[41]

In a very interesting paper published in 1887 Weichselbaum reported the results of the bacterioscopic examination in eight cases of meningitis, in the first two of which he isolated the pneumococcus. He observed, as did also the present writer, that injection of pneumococci into the cranial cavity might produce meningitis. In the six other cases he did not find the pneumococcus, but he isolated other microorganisms having the form of cocci, or, better, of hemispheres, ordinarily grouped in twos with the plane surfaces apposed. These microbes were sometimes free in the exudate, but more commonly they were found within the cells. To this new microbe Weichselbaum gave the name of diplococcus intracellularis meningitidis, and attributed considerable importance to its action.

Goldschmidt[52] in the same year at Nuremberg found the same micrococcus in a case of cerebrospinal meningitis. Netter[122] also found it in 1887 and 1888, and the same microbe was found by Jaeger[74] during an epidemic occurring in the army of Würtemberg in 1893–94. The same microbe has also been isolated in Moscow, Vienna, Königsberg, Berlin, Kiel, Munich, Cologne, Budapest, Amsterdam, and Boston.

In addition to these two microbes found in cases of cerebrospinal meningitis, Bonome,[15] of Padua, found a third, to which he gave the

name of streptococcus capsulatus meningitidis (Figs. 6, 7, and 8). The microbe occurred in the form of chains, and in cultures it was enveloped in a capsule. Bonome regarded this microbe as different from the pneumococcus, and he defended his opinion in a rather long discussion held with Foà and Uffreduzzi.

We propose to study these microbes to which an important rôle in the pathogenesis of cerebrospinal meningitis has been assigned.

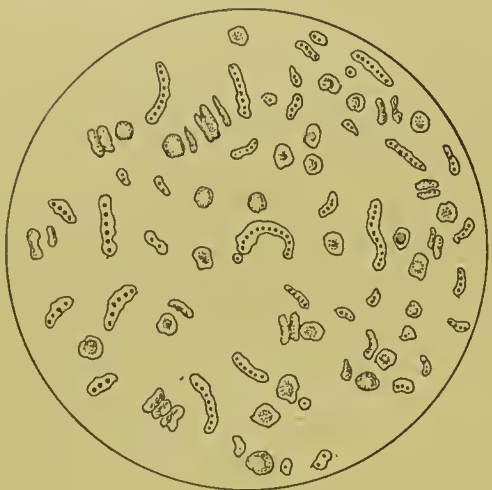

FIG. 6.—Blood of a Rabbit Inoculated with Bonome's Streptococcus.

FIG. 7.—Culture of Bonome's Streptococcus in Bouillon.

We shall indicate their principal characters, and shall see on what grounds the belief in their pathogenic action is based. And finally we shall seek to establish their relative importance and the relation they hold to each other.

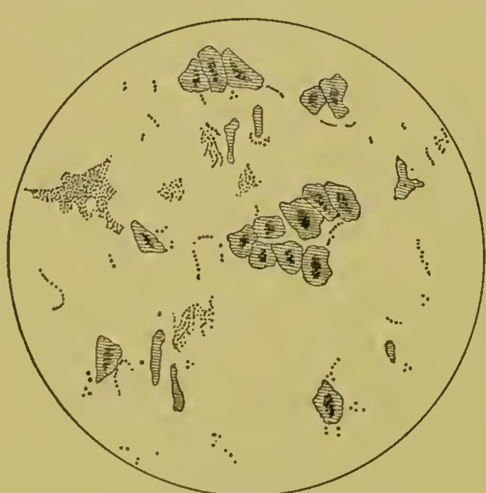

FIG. 8.—Streptococcus of Bonome; pus from a case of meningitis.

THE PNEUMOCOCCUS.

The pneumococcus found in cases of meningitis usually presents characters very similar to those it possesses in pneumonia. The cocci are usually enclosed in a very distinct capsule; the tapering, lance-shaped appearance of their free extremity is very marked; they are arranged as diplococci, but often form rather long chains in consequence of which they may be mistaken for streptococci. Their nature cannot, however, be misunderstood. They develop only at a temperature very nearly that of the human body.

The best media for their cultivation are gelose, on which they form transparent colonies compared to dew drops; and serum, either liquid or solidified. They are pathogenic in the case of mice and rabbits, these animals succumbing, when the inoculation is made under the skin, to a generalized septicæmia, with œdema around the point of injection and tumefaction of the spleen. Injection into the pleural cavity gives rise to a double serofibrinous pleurisy with pericarditis.

Netter[xii] has produced cerebrospinal meningitis in rabbits by inoculating them with cultures of the pneumococcus or with fluids taken from animals suffering from a pneumococcic infection. The inoculation was made in different cases into the cranial cavity, the spinal canal, the thorax, and into the blood. Weichselbaum[173] published in the same year experiments having similar results. We have already seen that the pneumococcus has been found in numerous epidemics, of which the following are some: 1886, Paris, Orléans (Netter[117]), Berlin (Fraenkel[44]), Bonn, Cologne (Leichtenstern[vi] and Ribbert[133]), Vienna (Weichselbaum[172]), Turin (Foà and Uffreduzzi[42]); 1887, Königsberg (Ortmann[134]); 1888–89, Pavia (Monte[109]); 1891, Florence (Banti[102]); 1893, Lonaconing (Flexner and Barker[41]), Carlsruhe (Panienski[137]), Tübingen (Henke[62]); 1893–94, Montpellier (Grasset[58]); 1894, Algiers (Scherb[150]); 1895, Sassari (Righi[151]); 1896, Recalnato (Vicenzi), Genoa (Jemma[76]); 1897, Hamburg (E. Fraenkel[95]); 1898, Paris (Netter[127]).

The pneumococcus in the meningitic exudate may present quite notable differences in virulence, and often it is not pathogenic for animals immediately after being obtained from the human body, but must be strengthened by a rest for a time in the cellular tissue (Ortmann) or by culture in serum for twenty-four hours. During the last epidemic it was observed that a subcutaneous injection into mice of the pneumococcus obtained from cases of meningitis did not kill them, while the virulence of the microbes was evident when the injection was made into the peritoneum or pleura.

I have already spoken of the arrangement in long chains which the pneumococcus often assumes in the meningitic exudate, an arrangement which may persist even in the cultures.

The *streptococcus meningitidis capsulatus*, found by Bonome in six cases in the course of an epidemic at Padua in 1889, ought, it seems to me, to be regarded as simply a form of the pneumococcus. During the epidemic of 1898, indeed, I found in most of the cases a microorganism corresponding to the one described by Bonome, for it often formed long chains in the exudate. After cultivation in fluid serum and after successive passages through the organism of the white rat, this

microbe had all the characteristics of the typical pneumococcus lanceolatus capsulatus.

Henke in Tübingen found in one case a pathogenic streptococcus with which he produced all the symptoms of meningitis by inoculation after trephining in a rabbit. He regarded this streptococcus as a variety of the pneumococcus.

Diplococcus Intracellularis.

The diplococcus intracellularis meningitidis of Weichselbaum resembles in appearance the gonococcus, being disposed in pairs of hemispheres with the plane surfaces turned towards each other. It is decolorized by Gram's method. It is generally contained within the cells and may be found there in great numbers; but it is also found in a free state. Cultures are obtained with difficulty, and even when the exudate contains large numbers we find only a few colonies at the most. It can be cultivated only at the temperature of the human body. Weichselbaum employed agar-glycerin on which the microorganism forms grayish colonies, which are at first of small size, but may attain a diameter of three millimetres. The best culture medium is the serum-gelatin of Loeffler mixed with three parts of sheep's serum and one part of bouillon to which glucose has been added. On this medium thicker opaline colonies are formed. In cultures the meningococcus has the shape of a tetrad and is very rarely disposed in chains (Jaeger).

The meningococcus retains its vitality for a short time only at ordinary room temperature, and in order to preserve it, it is necessary to make successive transplantations at short intervals. In the oven, however, Weichselbaum has seen the microorganisms alive after eighty days. Heubner and others have cultivated the meningococcus in gelatin and found that it retains its virulence in this medium for quite a long time.

The meningococcus (diplococcus intracellularis of Weichselbaum) is not pathogenic for mice when the inoculation is made under the skin. Weichselbaum has obtained positive results only after inoculation into the thorax or abdomen in white mice. At the end of three or four hours the animal is no longer able to walk, but lies on its back with the eyes closed and breathing rapidly. It dies at the end of from thirty-six to forty-eight hours, and in the serous cavity where the injection was made is found a red viscous fluid and the spleen is increased in size. The microbe is so feebly pathogenic for other animals commonly used for experiments, such as rabbits, guinea-pigs, and dogs, that Jaeger and Councilman were led to believe that animals generally

resist its action on inoculation, but Heubner produced cerebrospinal meningitis by inoculations of cultures into the spinal canal of the goat. Kiefer,[79] while making investigations with the diplococcus, was attacked with a violent coryza which extended to the sinuses and was accompanied by general symptoms.

Relative Importance of the Pneumococcus and the Diplococcus Intracellularis.—Certain observers, and more particularly Jaeger and Heubner, believe that the diplococcus intracellularis is the sole pathogenic agent in epidemic cerebrospinal meningitis, and that the pneumococcus has no influence whatever in the production of true epidemic meningitis. Councilman[1x] is a little less emphatic, although he appears disposed to adopt this way of thinking. I do not, however, in any way accept this view. The pneumococcus can without any doubt cause meningitis, and in spite of Heubner's experience, the rôle of the pneumococcus has been most surely established experimentally. The frequent occurrence of pneumonia complicating meningitis and of meningitis complicating pneumonia, and the coincidence with meningitis of many other inflammations which may be excited by the action of the pneumococcus, imply that between pneumonia and meningitis there exists a relation which cannot be denied. We shall return to this point later.

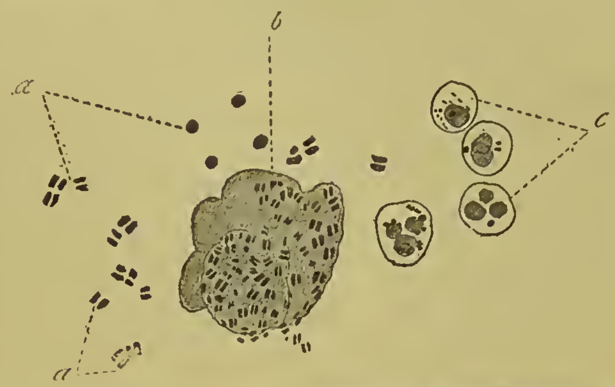

FIG. 9.—Diplococcus Intracellularis of Weichselbaum. *a*, Free diplococci; *b*, diplococci in an endothelial cell of the pleura; *c*, diplococci in cells in the meningeal exudate. (After Weichselbaum.)

Certain cases in which the diplococcus of Weichselbaum was found may really have been cases of pneumococcic meningitis. Thus in 1893 Jaeger is said to have found the diplococcus alone in the course of an epidemic among the Würtemberg troops, but inoculations showed that in some instances at least the pneumococcus was present. Henke, who studied one of these cases in which Jaeger met with the diplococcus, himself found only the pneumococcus. During the epidemic of the past year I found the diplococcus intracellularis in only a small number of my patients, 16 out of 39, and in 10 of these cases cultures and inoculation experiments revealed the presence at the same time of the pneumococcus. At Hamburg, Lenhartz examined the fluid obtained by lumbar puncture and found the diplococcus of Weichselbaum 13 times and the pneumococcus 9 times. In the same

city, E. Fraenkel made a bacteriological examination in 19 cases of suppurative meningitis and found the pneumococcus 12 times and the diplococcus of Weichselbaum once only. These results, which were obtained after autopsy when a very careful examination could be made, are of very great value, and I gladly record them here. I believe that the pneumococcus, being a very elusive microbe and requiring delicate procedures for its discovery, may have escaped the observation of many investigators.

It is even possible that the diplococcus intracellularis may be a degenerated form of the pneumococcus. In support of this view we may cite its intracellular position in evidence of a phagocytosis going on, the impossibility of cultivating most of the individuals as shown by the small number of colonies obtained, its decolorization by Gram's method, and its usual innocuousness in animals. I would not, however, insist upon this opinion or lay too much stress upon the arguments just mentioned, for the question is only hypothetical as yet.

Topography of the Meningococci in the Meninges and in the Various Organs.

We have yet to study the distribution of the pathogenic agents in the meninges and the rest of the body. Eberth noted their presence in the vessels and in the lymphatic sheaths, and the same has been observed by Foà and Uffreduzzi and by Flexner and Barker. In these observations the microbe was the pneumococcus. Councilman found the diplococci especially in the acute cases. They were contained in the cells, but rarely in large numbers. In the chronic forms a very careful examination was sometimes necessary, and very few of the organisms were found. There are always fewer in the spinal than in the cerebral meninges. In the acute cases Councilman found diplococci in the cells of the cortical substance and outside of the vessels and the meninges.

The pathogenic agents have also been found outside of the meningitic lesions. Foà and Uffreduzzi noted the presence of the microorganism in the accompanying pneumonia, in the inflamed peritoneum, pleura, and pericardium, and in the kidneys around the convoluted tubes and the glomeruli. Bonome has made similar observations, and Bozzolo and Jemma have found pneumococci in the blood taken during life from patients suffering from meningitis.

The diplococcus of Weichselbaum has been more rarely found outside of the lesions in the meninges, but Jaeger, Councilman, and various Austrian observers have been able to demonstrate its presence in the lesions of bronchopneumonia. It has been found also in the

pus of arthritis, in an abscess of the tonsil, in the discharge from the nasal cavity, and in the pus of an otitis. It does not seem to have been found as yet in the blood post mortem, in which fluid I found it three times during life.

I myself have found the agents of meningitis ten times in the blood (four times during life), once in the spleen, the kidneys, and the lymph bodies, three times in the lungs, once in the pleura and the pericardium, twice in the ear, once in the synovial fluid, and twice in the urine.

Microbic Associations.—In a very small number of cases observers have reported finding at the same time with the pneumococcus or the diplococcus the staphylococcus pyogenes, the streptococcus, the colon bacillus, the bacillus proteus, and the capsulated bacillus. These microbic associations are always secondary, however, and we must refrain from regarding any but the two agents above described as the primary causes of cerebrospinal meningitis.

Bacteriology of Sporadic Suppurative Meningitis.

It will be interesting to record here the results of bacteriological examinations in cases of suppurative meningitis occurring at other than epidemic periods. My investigations on this point were begun a long time ago. In 25 cases examined in 1888 [122] I found the pneumococcus 16 times (9 times when pneumonia was not present), the streptococcus pyogenes 4 times, the diplococcus intracellularis meningitidis 2 times, the encapsulated bacillus of Friedländer, a curved bacillus resembling the bacterium coli, and a very fine curved bacillus each 1 time.

To April, 1897, I examined 61 cases of meningitis, with the following results: pneumococcus in pure culture 35 times, the same associated with the streptococcus and with the staphylococcus each 1 time, the streptococcus alone 13 times, the diplococcus intracellularis meningitidis 3 times, the staphylococcus pyogenes aureus and the bacillus of Friedländer each 2 times, and the coli bacillus, the influenza bacillus, a fine bacillus, and a pyocyanic and saprophytic bacillus each 1 time.

As we see from the above the pneumococcus occupies the most important place in the bacteriology of sporadic suppurative meningitis. We also see the diplococcus intracellularis meningitidis figure in cases which presented unmistakably the characters of sporadic meningitis, and alongside of these two were found other microorganisms which have not been noted in epidemic meningitis. Many of the cases of streptococcic meningitis were secondary to a traumatism,

arose through extension of an inflammation from other parts, or occurred in the course of a pyæmia.

My results accord also with those which have been published by other observers. I need cite here only two sets of statistics. Malenchini,[102] a pupil of Banti, studied 13 cases of sporadic meningitis at Florence and found the pneumococcus 12 times and the streptococcus associated with the proteus once. The streptococcic meningitis was secondary to an otitis with necrosis of the temporal bone. The cases of pneumococcic meningitis could be subdivided into primary meningitis 8 cases, meningitis associated with pneumonia 2 cases, and meningitis associated with endocarditis and with endocarditis and peritonitis each 1 case.

Councilman, Mallory, and Wright examined 20 cases of sporadic meningitis at Boston, and found the pneumococcus 10 times, the bacillus pyocyaneus associated with the staphylococcus 1 time, another bacillus 1 time, and the streptococcus pyogenes 8 times. The cases of pneumococcic meningitis were isolated primary meningitis 2 cases, secondary to pneumonia 3 cases, associated with bronchopneumonia, with pericarditis, and with otitis each 1 case, and following trauma 2 cases. The cases of streptococcic meningitis were secondary to otitis 4 cases, and to erysipelas, puerperal infection, alveolar abscess, and fracture of the nose each 1 case.

We might multiply citations of this kind *ad infinitum.* They suffice to show that the pathogenic agents encountered in epidemic cerebrospinal meningitis are found also in sporadic suppurative meningitis, and that in the latter as in the epidemic form the pneumococcus plays the principal rôle. My own observations serve also to demonstrate that the diplococcus intracellularis meningitidis is by no means confined to epidemic cerebrospinal meningitis.

Comparative Pathology.

Comparative pathology furnishes us with some details which possess a certain interest. Cerebrospinal meningitis, either epidemic or sporadic, is sometimes seen in the horse and in the goat. In the disease as occurring in the horse some bacteriological examinations have been made.

Siedamgrotsky and Schlegel, in the course of an epizootic occurring in 1894–96 in the northwestern part of Saxony, found in four-fifths of the cases, examined by making cultures from the cerebral substance or the meningeal fluid, a coccus which was ordinarily single but more rarely a diplococcus, and which sometimes was collected in masses in the cells. This microbe produced no ef-

fect in rabbits and mice, but was pathogenic in the case of the horse.

Johne[77] examined twelve cases, in seven of which he made the autopsy himself, and observed the venous congestion of the meninges and areas of opacity with a transparent exudate containing but little albumin, about 150 gm. in amount; in the five other cases he examined the cerebrospinal fluid which was sent to him for this purpose. In all these twelve cases the cerebrospinal fluid contained in small quantities a small diplococcus which was cultivated readily on agar-glycerin and could be stained by all the reagents. It had the form of a biscuit, like the gonococcus, and was sometimes arranged in groups of four. It was surrounded by a sort of capsule. It occurred most commonly free in the exudate, but sometimes, though rarely, it was enclosed in the cells. Guinea-pigs died in thirty-six hours after intraperitoneal inoculation, with signs of intoxication, and the microbe was found in all their organs. Two goats in which he made intraspinal injections died, one after thirty-six hours, the other at the end of nine days. Upon section there were found in them the lesions of suppurative cerebrospinal meningitis, and the exudate contained these microbes either free or enclosed in cells. Two horses which were inoculated in the cord had symptoms of meningitis, but recovered. In one of them the symptoms were very marked and increased for five days, at the end of which time they began to decline. Johne believed that the microbe found in the horse resembles very closely the diplococcus intracellularis of Weichselbaum. No cases of meningitis in man were reported in the district in which this epizootic prevailed, but in spite of this we are justified in believing that there is a relationship between meningitis in the horse and that in man.

According to Carbonaro meningitis was carried from men to animals of the bovine and equine races in the little town of Canosa, near Naples. Boudin tells us that the lesions of meningitis were found in several artillery horses which died suddenly during the epidemic of meningitis at Grenoble.

Upham[169] tells us that in 1873 in several localities in Massachusetts there was during the course of an epidemic of meningitis a similar disease affecting horses. According to Flagg the animals were taken with pain and rapidly progressive swelling of the muscles of the sacrolumbar region, which then became rigid and hard as steel. A little later this rigidity yielded to flaccidity with loss of strength. In one case the muscular weakness existed on one side only, and in several cases it was more marked on one side than on the other. In eight of the animals there was opisthotonos, and in three the muscles

of the nucha were swollen. One animal had paralysis of the optic nerve. Three of the horses died, and at autopsy the muscles were found congested, and the spinal meninges were inflamed and the seat of ecchymoses and exudation.

Lewis Smith[162] tells us that an epizootic of the same nature prevailed in New York among the omnibus horses in 1871, prior to the appearance of an epidemic of meningitis.

EPIDEMIOLOGY.

Opinions have differed widely concerning the nature and the conditions of the spread of cerebrospinal meningitis. Some writers regard the disease as extremely contagious and calling for the most rigorous preventive measures. Others deny that it is in any sense contagious and regard it as a purely miasmatic affection or a simple local inflammation. Others, again, deny that it is an independent disease, regarding it simply as a form of typhus fever. These differences of opinion become explicable if we think of the various appearances of the different epidemics, as we may see from the following sketch.

In America and in Sweden certain visitations of meningitis have presented the classical type of the great epidemics of the Middle Ages, invading within a brief period extensive territories and attacking a large number of individuals. These epidemics may also prevail for several years. In Sweden, for example, meningitis prevailed in

1855	in	6	provinces,	35	communes—	3,000	cases,	886	deaths.
1856	"	9	"	44	"	2,000	"	428	"
1857	"	16	"	157	"	3,051	"	1,387	"
1858	"	19	"	113	"	1,909	"	779	"
1859	"	18	"	77	"	1,415	"	582	"
1860	"	12	"	32	"	347	"	148	"
1861	"	9	"	11	"	91	"	27	"

If we regard these figures without entering into an analysis of them it would appear that the epidemic of meningitis was of very long duration. In reality, however, each summer the meningitis was almost completely arrested, but it reappeared in the winter. Furthermore, the disease progressed from the south to the north, stopping each year at a point about 1.5° to 2° of latitude above its limit of the previous year, and the same locality was visited at the most two years in succession.

In the first American epidemics, and also in Germany from 1863 to 1867, the progress of the disease was very similar. Usually in

these extensive epidemics in Sweden and America the disease seemed to advance without any special connection with the relations existing between the different localities, and often it was impossible to determine how the infection was imported. In Germany, however, this was not always the case, and in certain districts in the centre and south of Germany the first cases were in people who had recently come from the eastern part of Switzerland or from Silesia, which were the first regions invaded.

In regard also to the French epidemic of 1836 to 1848, if we look only upon the entire extent of country involved, we shall conclude that it was of even longer duration than the Swedish visitation. But if we follow its progress on the map we shall see that it advanced, not as an army corps with serried ranks, but rather irregularly and without any apparent order, like squads of skirmishers. Each year new territories were invaded, and these were in different parts of the country, some in the east and some in the west, and everywhere or nearly everywhere the limits of each invaded area were sharply drawn. Only one city would be attacked, and sometimes only one portion of a city. But the interesting local reports and the general histories of Broussais and of Boudin give us the key to this apparently mysterious disposition. The epidemic was confined almost exclusively to the troops, and it was to the frequent transfers of the garrisons, common at this period in France, that the successive invasions of cities distant one from the other was due. An interesting fact in this connection is that in almost all these places the disease did not spread outside of the barracks, and the civil population of the cities remained as a rule free from infection. Almost the only exceptions to this rule were in the Department of Landes, which was the original starting-point of the epidemic, and the city of Aigues-Mortes, where the disease made great ravages among the civil population. In Strasburg a few civilians were attacked. In Rochefort in 1838–39 the epidemic of meningitis was almost wholly limited to the convict prison. In Paris in 1848 there was a small epidemic in one of the prisons which coincided with a greater one confined to the troops.

We have here seen two quite distinct types of epidemic, and we may add to them a third type, one in which the epidemic is of very limited extent, attacking one city only or one village, or prevailing in only a single part of the city or in one street or even in one house. In these limited epidemics occurring in small towns it is often impossible to trace the means of importation, but it is often possible on the other hand, as Frew and Galton have done, to establish the fact of a relationship between the cases observed. In epidemics occurring in prisons, barracks, and hospitals (as in the foundling hospitals at

Vienna and at Stockholm) the mode of contagion may be absolutely undiscoverable, and being unable to refer it to an importation we may be driven to establish a relation with some previous epidemic, possibly many years before. Finally in the limited epidemics occurring in large cities it may be impossible to determine the mode of importation or to trace any connection between the different cases.

At first sight all these facts seem to be most contradictory, and there is apparently no way of reconciling them. We purpose making the attempt, however, and in order that our study may be more fruitful we shall pursue it in the following order. We shall first take up the accepted facts concerning the disease, such as the size of the epidemics, their duration, the date of their appearance, the influence of soil, etc., the individual causes (age, sex, etc.), and the occasional causes. After that we shall study the contagious nature of the disease, the arguments which have been advanced in support of it, and the usual modes of contagion, and we shall also examine into the reasons why the affection is usually only mildly contagious. From this study we shall learn that the various peculiarities of the disease are in relation with the properties of the infectious agent of meningitis. We shall then see whether an epidemic of meningitis may arise spontaneously, and also whether there exists any essential difference between epidemic and sporadic meningitis. Finally we shall examine into the question of the relation existing between cerebrospinal meningitis and pneumonia and that of the unity or plurality of epidemic meningitis, and shall conclude our labors with a discussion of the important subject of prophylaxis.

Etiology.

Epidemic Extension.—Although one of the most dangerous of diseases to those who are attacked by it, the mortality varying from three-quarters to all of those attacked, cerebrospinal meningitis, since the beginning of the present century at least, has nowhere made such ravages as have most of the infectious diseases, indigenous or exotic. Usually an epidemic of the disease causes but slight increase in the total mortality, and the number of people attacked by the disease is small in proportion to the general population. The epidemics of Lippusch (near Dantzig), in which 12.5 per cent. of the inhabitants were attacked, and that of Aigues-Mortes, in which the sick numbered 160 out of 3,000, were exceptional. At Strasburg, in 1841, the proportion of sick was only 3 in 1,000; in Cologne, in 1885, it was 1 per 1,000; in Copenhagen and Boston the proportion was even smaller, and in the large cities of Berlin, Vienna, and Paris it was quite insignificant.

If, however, instead of studying the morbidity statistics of a country or a large city, we examine into what takes place in a barrack, a house, or a room, we shall find very contradictory results. This question will be discussed more profitably later, and here we need only retain the fact that epidemics of cerebrospinal meningitis are ordinarily of limited extent.

Duration.—As a general rule the disease does not remain long in a locality—a few months at the most. The epidemic rather rapidly attains its maximum, and we are able to recognize in it the three periods of increase, rest, and decline. At Versailles, in 1839, the disease appeared during the first days of February, reaching its maximum almost immediately, and ended in June. In February there were 72 cases out of a total of 154; of these 17 were between the 4th and the 10th of the month, 41 between the 11th and the 20th, and 14 between the 21st and the 28th. In March there were 26 new cases, 17 in April, 27 in May, 11 in June, and 1 on July 15th.

The epidemic at Aigues-Mortes lasted three months.

At Strasburg, in 1840–41, the epidemic in the garrison lasted nine months, the cases being distributed as follows: Period of increase, 12 (October, 1; November, 3; December, 8); period of rest, 142 (January, 34; February, 43; March, 65); period of decline, 42 (April, 29; May, 9; June, 4).

In Copenhagen the epidemic lasted from December, 1885, to August, 1886, the cases being divided as follow: Period of increase, 13 (December, 4; January, 2; February, 7); period of rest, 73 (March, 17; April, 35; May, 21); period of decline, 23 (June, 15; July, 3; August, 5).

In Boston the disease prevailed from December, 1896, to September, 1897, the admissions to hospital being the following: Period of increase, 14 (December, 3; January, 1; February, 10); period of rest, 73 (March, 23; April, 29; May, 21); period of decline, 24 (June, 14; July, 7; August, 0; September, 3).

In Cologne the epidemic lasted from January to November, 1885, the cases being distributed as follows: Period of increase, 19 (January, 1; February, 3; March, 15); period of rest, 70 (April, 27; May, 22; June, 21); period of decline, 19 (July, 4; August, 4; September, 8; October, 2; November, 1).

These examples will suffice to show that the general formula is repeated everywhere, namely, an epidemic of moderate duration, with three distinct periods.

There is another very interesting point of which we have to make mention here, namely, the possibility of a *recrudescence* of the epidemic after a period of abeyance of longer or shorter duration. Thus

in Strasburg in the epidemic of 1840-41, the disease completely disappeared in July and August, but returned in September, and caused sixteen deaths between that time and December. At Helsingfors there were 13 cases of meningitis at Runeberg's clinic in 1885 (from March to December) and 12 in 1886 (from January to August). At Cologne there was a recrudescence of the epidemic in December, 1885, and from that time until the end of June, 1886, there were 37 cases.

We may profitably study a little more closely the figures relating to cerebrospinal meningitis in Cologne from 1885 to 1892, as given by Leichtenstern. There were in 1885, 111 cases; in 1886, 34 cases; in 1887, 4; 1888, 26; 1889, 5; 1890, 4; 1891, 4; 1892, 6. From these figures we see that the disease lost its epidemic character in 1887, and that the cases occurring from 1889 to 1892 may fairly be called sporadic, but that in 1888 the number of cases was sufficiently large to deserve the name of a small epidemic. The statistics of New York and Boston are of a similar nature. Thus in New York from 1872 to 1882 we find in

1872, 782 deaths.	1876, 127 deaths.	1880, 170 deaths.
1873, 290 "	1877, 116 "	1881, 461 "
1874, 158 "	1878, 97 "	1882, 238 "
1875, 146 "	1879, 108 "	

From these figures we see that the disease prevailed during the whole period, but that there was a new epidemic in 1881, nine years after the first.

In Boston the statistics embrace a much longer period. There were in

1865, 2 deaths.	1873, 216 deaths.	1881, 16 deaths.
1866, 0 "	1874, 35 "	1882, 24 "
1867, 7 "	1875, 41 "	1883, 23 "
1868, 8 "	1876, 13 "	1884, 26 "
1869, 7 "	1877, 24 "	1885, 19 "
1870, 5 "	1878, 19 "	1886, 14 "
1871, 3 "	1879, 15 "	1887, 16 "
1872, 60 "	1880, 9 "	

Townsend,[168] in commenting upon these figures, draws the conclusion that cerebrospinal meningitis may become endemic, but the history of the invasion of 1897 shows that places in which the disease has become endemic may be the seat of epidemic recrudescences. And this leads us to the conviction that the cases of sporadic and of epidemic meningitis in these localities have the same origin and are of the same nature. We shall refer to this again when we come to a discussion of the relations between sporadic and epidemic meningitis, and we shall see that testimony of the same character is presented to us by the clinical history, pathological anatomy, and bacteriology.

Seasonal Distribution.—Cerebrospinal meningitis is a disease of winter and spring, as is shown by the tables above given of the epidemics occurring in Versailles, Strasburg, Copenhagen, Cologne, and Boston. Meningitis appeared in winter also in Geneva (1805), Denmark (1845), Sweden (1855), Silesia (1863), Gibraltar (1864), and Portugal (1861 and 1862). Additional evidence is furnished by the two following tables. The first table is from Hirsch, and shows the time of occurrence of a large number of local epidemics in France and Sweden.

	France.	Sweden.		France.	Sweden.
December	26	19	Winter	97	119
January	32	45			
February	39	55			
March	30	65	Spring	69	192
April	23	68			
May	16	59			
June	16	37	Summer	30	64
July	7	16			
August	7	11			
September	8	8	Autumn	30	22
October	10	6			
November	12	8			

The following table is constructed from the figures collected by Sievers from the official mortality statistics of Sweden and Norway:

	Sweden, 1855–1884.	Norway, 1866–1882.
January	468 deaths.	67 deaths.
February	576 "	113 "
March	767 "	154 "
April	779 "	142 "
May	474 "	160 "
June	328 "	112 "
July	218 "	61 "
August	155 "	40 "
September	132 "	28 "
October	146 "	33 "
November	176 "	21 "
December	164 "	36 "

In the presence of a predominance so distinctly accentuated as this we might be led to assume that the temperature played a favoring rôle in the etiology of cerebrospinal meningitis; in other words, that it was a disease *a frigore*. In many patients, as we shall see below, meningitis occurs after a chilling of the body, but these cases are exceptional. The winters in which epidemics of meningitis have occurred have not been characterized by especially cold weather, and indeed in many instances the epidemics have occurred in the course of an exceptionally mild winter.

The degree of humidity, the variations of atmospheric pressure, the prevailing direction of the winds, etc., are all factors which do not appear to influence the predilection of meningitis for the winter and spring months. As in the case of pneumonia, it is probable that we must attribute the increase in the virulence of the pathogenic agents to some element as yet unknown.

Several authors have recorded the appearance of meningitis in damp localities similar to those in which malaria prevails. At Aigues-Mortes the epidemic appeared after quite extensive floods, according to Schilizzi, and in Piedmont, in 1839, meningitis prevailed especially in the rice-swamps (di Renzi). Upham in 1862-63 recorded an epidemic of cerebrospinal meningitis among the Federal troops encamped in the marshy regions along the Potomac River. A more complete study, however, shows us that epidemics have prevailed in all regions, on elevated plateaus as well as in the plains, in places with sandy or rocky soil as well as in those with alluvial soil.

Crowding and *defective local hygiène* have been often noted in places where epidemics occurred. But meningitis has persisted in bodies of troops, in spite of their removal to other quarters, and in many garrisons it has seemed to prevail most extensively in those barracks which were apparently the most healthful. It would be very easy to multiply cases of this sort. Although it is true that in cities the cases of cerebrospinal meningitis occur in greatest numbers in the narrow streets, where the houses are less well ventilated, and where the population is most dense, there is nothing in this that we do not see in the case of any epidemic infectious disease.

Meningitis occurs at all *ages*. The following are the statistics bearing on this point collected by Leichtenstern: Of all cases there occurred in persons

Under 1 year	3	
Between 1 and 2 years	3	
“ 2 “ 3 “	3	Under 5 years, 17.
“ 3 “ 4 “	4	
“ 4 “ 5 “	4	
“ 5 “ 10 “	14	
“ 10 “ 15 “	10	
“ 15 “ 20 “	19	
“ 20 “ 25 “	18	
“ 25 “ 30 “	10	
“ 30 “ 35 “	6	
“ 35 “ 40 “	6	
“ 40 “ 50 “	5	
“ 50 “ 60 “	5	
“ 60 “ 70 “	1	

In Massachusetts the deaths from cerebrospinal meningitis between 1887 and 1895 were divided as follows:

Under 1 year	316	Under 5 years, 676.
Between 1 and 2 years	146	
" 2 " 3 "	99	
" 3 " 4 "	77	
" 4 " 5 "	38	
" 5 " 10 "	132	
" 10 " 15 "	81	
" 15 " 20 "	61	
" 20 " 60 "	186	
Over 60 years	43	

We see from these figures that meningitis is comparatively rare after the age of thirty years, but the two sets of statistics differ somewhat, in that the German figures indicate that the age most exposed to an attack of the disease is that between fifteen and twenty-five years, while the American table shows that the greatest number of cases in any quinquennium are found in the first, and that more cases occur during the first year of life than in any other.

Sex does not appear to be of any importance whatever in the etiology of cerebrospinal meningitis.

General Health.—Chauffard, di Renzi, Hirsch, and most other authors have observed that cerebrospinal meningitis attacks by preference robust persons, resembling in this respect pneumonia. Among one hundred and twenty-four patients seen by Leichtenstern in Cologne between 1885 and 1892, there was not one with tuberculosis or scrofula. My own observations, however, have shown the rather frequent occurrence of mixed meningitis (cerebrospinal meningitis in which the tubercle bacillus is found), so that I cannot accept Leichtenstern's belief in the immunity of the tuberculous. Nevertheless, my patients, especially those in private practice, were for the most part vigorous and in usually good health.

Cerebrospinal meningitis occurs with greatest frequency in persons who are *overworked* mentally and in those suffering for the time being from physical or nervous depression. These two influences are united in young soldiers, and this explains the unusual frequency with which such are attacked by the disease. In Versailles in 1839 the raw recruits furnished 66.5 per cent. of the cases and 85 per cent. of the deaths. This proportion is larger even than it seems, if we consider the general composition of the French army at that time (Faure Villars).

At Metz, out of 48 patients, 36 had had less than one year of service, 8 from one to two years, 2 from two to three years, 1 from three

to four years, and 1 over five years. Of 46 soldiers treated by Tourdes, 30 had been with the colors less than one year.

In many cases some *disappointment* or strong *emotion* has been recorded as having been experienced by the patient before falling ill. J. Lewis Smith reports the case of a girl of ten years who came home from school in tears after having failed in her examination. That same evening after finishing her lessons she was seized with fever and cephalalgia, which marked the beginning of an attack of meningitis. Another case occurred in a woman who had become greatly fatigued in fitting up a shop which she was about to open on Broadway, and who was also anxious as to the result of her venture.

The influence of *cold* appears very distinctly in the report of an epidemic at Lonaconing published by Flexner and Barker. The two first patients to suffer in this locality were seized the day following a ball. They had danced a great deal and had passed from the ball-room while bathed in perspiration into an icy temperature outdoors. Smith reports the case of a lad who was attacked on the day after having bathed in the Hudson River when greatly fatigued.

Tourdes regards the *abuse of alcohol* as a probable factor. Albert Robin has shown that delirium tremens may be accompanied by meningitis, and Rabjean has reported three cases, observed in one hospital service within six weeks, of alcoholic subjects admitted for delirium tremens in whom suppurative meningitis existed.

Insolation has been occasionally instanced as an etiological factor.

Traumatisms, and especially injuries of the cranium, are deserving of particular mention in a discussion of the etiology of cerebrospinal meningitis. Such injuries may, of course, at any time be followed by meningitis, but this result is vastly more common during an epidemic prevalence of the disease. Sewall[160] reports an interesting series of cases which were among the first, if not the first, occurring in New York in the year 1872. A boy, Albert Brown, was pushed by one of his playmates and struck his head against a railing. The injury appeared insignificant, the child scarcely complaining of it at all, but in the evening he began to suffer from headache, and he died the following day. After him five of his brothers and sisters were attacked with meningitis, and four of them died. Ziemssen, Mannkopf, Strümpell, Kornfeld, Weiss, and Scheerer have all reported similar cases, and it is important in a medicolegal sense as well as in a clinical one to know of the existence of such cases.

Among those especially liable to suffer from cerebrospinal meningitis are patients with tumors, old hemorrhagic centres, softening, or other disease of the brain or cord. These alterations are to be regarded as exciting causes, as they diminish the resisting powers of

the nervous centres. Cases illustrating this have been reported by Immermann, Netter, and Klippel.

Coincidence with Other Epidemics.—An epidemic of cerebrospinal meningitis has often coincided with one of influenza. We know that there exist close relations between influenza and pneumonia, which we may explain by the fact of the pathogenic activity of the pneumococcus being increased during the epidemic prevalence of influenza. Epidemics of cerebrospinal meningitis have sometimes coincided with those of scarlet fever (Laveran, Lemoine), but such coincidences, which have been noted only exceptionally, do not point to any intimate relation between the two affections, and few share the opinion of Laveran who regards cerebrospinal meningitis as caused by the poison of scarlatina.

Contagion.

The most important question, as regards prophylaxis, is that of the contagiousness or non-contagiousness of cerebrospinal meningitis. At the period when it prevailed to the greatest extent in France the believers in contagion were few, most authorities refusing to regard the disease as of contagious nature. Tourdes thought that meningitis arose from a miasmatic infection favored by overcrowding. He believed that all the facts argued against the presumption of contagion. Forget, who observed the same epidemic at Strasburg, denied absolutely the possibility of contagion, and Levy the same at Paris.

Boudin alone, beginning with his earliest works, defended with great conviction and by means of forcible arguments the doctrine of contagion in cerebrospinal meningitis. The arguments which he brought forward were the following: 1. A frequent coincidence of the appearance of the malady with the arrival of troops from some locality where the disease prevailed or had just prevailed. 2. Reproduction of the disease in certain regiments, notwithstanding their change of garrison. 3. The reappearance of the disease in certain garrison towns and sometimes in the same barracks, although the garrison had been changed. 4. Occurrence of the disease among physicians, nurses, sisters, and other hospital attendants, patients suffering from other diseases, children of the soldiers, camp followers, sutlers, etc. 5. Localization of the meningitis to regiments, barracks, houses, or families. 6. Limitation of the epidemic sometimes to the civil population, the troops escaping, and sometimes to the military population, the civilians and the inmates of military prisons enjoying an immunity. 7. The appearance of the malady in Algeria after it had existed in several of the southern cities where there were depots for the Algerian troops. 8. Immunity of Switzer-

land and of the neighboring parts of France, notwithstanding the ravages of the disease in nearly all the frontier cities of France. Each of these arguments in Boudin's work is supported by many examples. Hirsch, Leichtenstern, and Laveran, although not so positive in the affirmative as Boudin, nevertheless attribute to contagion an important rôle in the etiology of cerebrospinal meningitis, while Ziemssen and Strümpell are non-committal. Wolff again denies the agency of contagion, and Councilman appears to hold the same opinion.

I believe that the contagiousness of cerebrospinal meningitis is indisputable, and that this is the most essential etiological factor. We may now profitably discuss the proofs upon which this belief rests. It will be necessary to select our examples from the various epidemics in such a way as to anticipate a question already indicated and to which we shall return, namely, whether all the epidemics of meningitis are the expression of one single disease, of one single pathogenic agent, or whether a contagious, a sporadic, and a miasmatic disease have not all been included under one title. We shall study these various arguments in the following order: 1. The transmission of the disease to persons whose profession calls them to care for those suffering from the same affection. 2. The succession of many cases in the same family or among those living in the same house. 3. The importation of meningitis into a country, a definite locality, or a part of a city. 4. The progress of the disease in a locality where it has gained access. 5. The immunity of bodies of people living under the same conditions as those suffering from the epidemic visitation but who have and can have no communication with the latter.

1. In many epidemics the persons who have had the care of the sick have been attacked. Examples of this are doubtless less numerous than in the case of typhus fever, but they are no less demonstrative. At Grenoble[27] in 1814, at Rochefort[92] in 1839, at Avignon[23] in 1840, at Strasburg[11] and at Schlestadt in 1841 there were cases of meningitis among the physicians, the sisters, and others of the hospital personnel. These cases are reported by Boudin, but we prefer to take our examples from other epidemics. And first the observations of Leichtenstern in the hospital at Cologne. In this hospital a sister and three nurses who had had charge of the patients with meningitis were attacked by the disease. Three of these had not gone outside of the hospital for a long time and could not have acquired the disease beyond the walls of the building. These facts brought forward by Leichtenstern are the more demonstrative, as the personnel of the wards where no cases of meningitis were received furnished no

cases of the disease. Montanari[108] tells us that in the hospital at Foggia, where the soldiers suffering with meningitis were treated, a nurse and two young women in the building were attacked.

2. We have very many instances of the multiplicity of cases of meningitis in a family or among the inmates of one house. One of the most convincing of such instances and one which appears to have escaped the notice of European epidemiologists, is that of the Brown family, reported by Sewall.[160] At the beginning of the epidemic in New York in 1872, six of the children in this family were attacked in the following order: Albert, 7 years old, was taken ill January 30th, died; Max, 4 years old, February 4th, died; Theresa, 13 years old, February 6th, recovered; Berthold, 11 years old, February 7th, died; baby, 19 months old, February 10th, died; Henry, 5 years old, March 16th, died.

Although Sewall does not think that contagion was active in these cases I cite the example in support of this theory, for in no contagious disease could we ever find a greater accumulation of cases. I do not deny that similar cases are the exception in cerebrospinal meningitis, but there are very many instances in which two or three members of the same family have been attacked at short intervals. Morcieca, quoted by Thorne Thorne,[166] saw in the Island of Gozzo (Malta) seven cases of meningitis in a family of nine persons. Kohlmann[85] reported in 1889 the history of a family in which the father was attacked on December 19th, a son on January 9th, and a daughter some days later. Müller[110] in Gotha in 1897 attended two brothers seized the one a few days after the other. Montanari in the epidemic at Foggia noted that of nine soldiers suffering from the disease eight belonged to the same mess. Among my personal cases in 1898 I saw meningitis attack at intervals of a few days a mother and her son, and in another house two children, and my colleague Ménétrier saw two brothers attacked at the same time. It seems unnecessary to cite any more examples of this sort.

3. The facts pointing to the importation of cerebrospinal meningitis into a country, district, or quarter of a city are, in my opinion, the most conclusive of all concerning the contagiousness of the disease, and I shall dwell upon them at some length. It has been shown in the section on the history that we were justified in believing that the French army had thus introduced meningitis not only into Algeria in 1840, but also into Italy, where the disease appeared first at Ancona which was occupied by a French garrison. It was also shown that the same regiment, the eighteenth of the line, had introduced cerebrospinal meningitis into Versailles and Rochefort, and that the disease was brought to Strasburg in October, 1840, by the seventh regiment

of the line, four members of which had died of meningitis on the way.

At Berlin in 1864 the first case of meningitis was observed on February 9th, in the person of a reserve of the Alexander regiment, which had come the last of January from Liegnitz, where there had been an epidemic in 1863. Five cases followed this one in the same company. Niemeyer attributes the appearance of cerebrospinal meningitis in Rastadt to the arrival in this federal fortress of recruits coming from Northern Germany.

At Foggia meningitis was introduced in 1893 by recruits who had come from Viesto where the disease prevailed in 1892 (Montanari). De Moulon saw seven cases of cerebrospinal meningitis in the suburb of San Vito at Trieste, among the families supplied with milk by a woman living at Noghera, where the disease prevailed.

Hirsch justly lays great stress on the following observation which he regards as the most demonstrative among all the facts collected by him during the epidemic of meningitis in Eastern Prussia in 1865: A person named K. fell ill at Szczakau on February 8th. A young woman, W., from the village of Sullenczin was brought to take care of him. After the death of K., W. returned to Sullenczin, and died of meningitis on February 26th. Previous to that time there had been only one case of meningitis at Sullenczin, that one occurring on January 19th. The administrator's family came from Podgass to assist at the funeral of W. Accompanying this family was a servant, D., and a child, O. A few days after the return from the funeral a daughter of the administrator was taken with meningitis and died in twenty-four hours. The domestic D. and the child O. also died, the first on the 4th and the second on the 7th of March.

At Rochefort in 1839 cerebrospinal meningitis appeared in the convict prison. The disease next seized upon the workmen in the shops in close proximity to the arsenal and the inhabitants of the houses in the immediate neighborhood. At Strasburg, Schlestadt, and Metz the first cases among the civil population were observed in persons living in the streets nearest to the barracks.

4. The apparently irregular distribution of cases of cerebrospinal meningitis in any given locality has often been traced to contagion. At Schlestadt Mistler found the first cases in the civil population in the persons of the child of the landlady of a cabaret frequented by the soldiers and of two children of a butcher who supplied meat to the garrison. In a small epidemic observed by Frew at Galton, five miles from Kilmarnock in Scotland, there were six cases between January 12th and March 27th, 1884. The six patients lived in five separate houses, but the author was able to trace a connection between the

different cases. The family of the first patient carried milk to the family of the second and third patients, a brother and sister attacked February 14th and 19th respectively. The fourth patient had been in the house of the preceding. The families of the fifth and sixth patients had had intercourse with the family of the fourth patient.

Richter[148] in 1886 reported the following case: Regina B—— came on October 17th to visit in a family where there were two children ill with meningitis. She passed the day there and then went to live with her uncle, in whose house she showed the first symptoms of the disease on October 21st. On November 9th, when convalescent, she received secretly a visit from a young man who brought her some dainties. On November 10th this young man showed the first symptoms of an abortive attack. He was able to return to the office where he was employed on November 19th, and on the 29th of the same month his neighbor in the office was taken ill with meningitis.

In large cities it is much more difficult to carry on an investigation of this sort, but Petersen succeeded in doing so in regard to the first cases of meningitis occurring in Berlin, these cases being apparently scattered all over the city without any order whatever. Out of twenty-six undoubted cases treated in hospital, in which the diagnosis was confirmed by autopsy or by the results of lumbar puncture, he was able to trace a direct or indirect relation with infected houses in sixteen.

5. Cerebrospinal meningitis spares collections of men living in the neighborhood of centres of the disease but having no possible communication with the sick. During the French epidemic the disease remained for the most part confined to the garrisons. Even in a single garrison it might remain confined to certain barracks or to the members of one mess. At Metz, where there were 76 patients out of a total of 7,841 men, or 1 in 76, or even 1 in 68, counting only the six corps which suffered most from the disease, there was not a single case among those detained in the military prison. While in 1840-41 there were many cases of meningitis among the garrisons at Strasburg and other towns in Alsace, in the neighboring Grand Duchy of Baden there was not a single case among either the military or the civil population. On the other hand, cerebrospinal meningitis began in December, 1864, at Rastadt and in the early part of 1865 almost all of Baden was invaded while no case occurred in Alsace.

Modes of Contagion.—Certain observations which have been made enable us to determine with a fair degree of certainty the manner of contagion of meningitis. These observations show the very curious detail that in most cases the disease is transmitted by means of objects which have become infected through contact with the sick.

A case observed by Kohlmann[85] is very conclusive. This author saw the disease in two families between the members of which there was no communication. In the first family (M.) there were three patients who were taken ill on December 19th. In the other family (B.) the meningitis appeared on December 29th, and a second case occurred on February 2d. The disease was introduced in the following way: The child of a poor family had returned from Godesberg ill on August 29th; it died of meningitis on the ninth day and was buried on September 6th. In order to appear decently clad at the funeral the parents borrowed clothing from the families M. and B., and they kept these clothes in their house for some days after the ceremony before returning them. The two members of the families M. and B., who were the first to fall ill, were precisely those whose clothes had been worn by the parents of the dead child.

Richter[149] cites the following case which is worthy of mention here: In the family C. two children, Gretchen and Rose, had had meningitis, the first on October 29th and the second on November 9th. They had not been brought in contact with any patients with meningitis, but a servant in the family had been burned and her burns had been dressed by a sister of charity who was nursing a patient with meningitis. This was an instance of transmission by means of a third healthy person. The same author saw a case of meningitis in a child whose father had not been ill but had closed the coffin of a person who had died of meningitis.

This infection by means of a third person who remains healthy, as well as that by means of objects which have been in contact with a person ill of the disease or which have been in the same room with this patient, establishes the fact that the contagium of meningitis may preserve its virulence after having left the body of the patient. The case reported by Kohlmann proves that this germ may remain active for a period of nine months. The contagium may be even more resistant than this, and it may remain active for several years. This explains how meningitis may reappear in the same place after the lapse of a long period, and also the fact that certain garrisons have become the seat of renewed epidemics after a long interval of immunity. Hermann and Kober have reported instances of meningitis recurring in a place after an interval of a year. During the period from 1837 to 1848 certain regiments had for several years in succession members attacked with the disease, although they had been changed to other garrisons. The explanation of these cases does not appear to me to be at all difficult, for in going from one place to the other the regiment carried the habiliments and arms belonging to those who had previously been ill with meningitis, and it was through contact with

these infected articles that the recruits, who each year partially changed the personnel of the regiment, acquired the disease. But all the effects were not moved with the regiment, and the localities themselves were contaminated. Certain recorded instances of the recurrence of meningitis in barracks show that the contagium of meningitis may preserve its vitality for a long period of time. At Bayonne from 1836 to 1897 meningitis appeared in seventeen different years, without counting nineteen during which there were probably some cases. The figures collected by Delvaille show that there were 3 deaths in 1836, 24 in 1837, 4 in 1838, 10 in 1839, 37 in 1840, 34 in 1841, 3 in 1842, 5 in 1843, 2 in 1848, 3 in 1849, 1 each in 1872, 1874, 1882, 1888, 1889, and 1896, and 9 in 1897.

Period of Incubation.—The wholly special conditions under which the virus of meningitis acts render it very difficult to determine definitely the duration of incubation in these cases. In certain cases in which this period could be determined with a fair degree of accuracy it was found to vary between three and eleven days.

Rarity of Contagion.—From what we have just seen, it can be asserted positively that cerebrospinal meningitis is transmitted by contagion; but there are certain peculiarities in this contagiousness. The degree of contagiousness is less marked than is that of most of the other infectious diseases. Indeed, instances of contagion in the wards of hospitals are very rare. Leichtenstern did not see a single instance of hospital contagion at Cologne, but this might be attributed to the precautions taken. At Strasburg, however, there were no precautions whatever, and yet Tourdes saw only 2 cases in which the disease attacked patients within the wards, although 80 cases of meningitis were treated there. In private houses single cases are the rule. In 160 houses in Cologne, where cases of meningitis occurred, in 10 only was a second case observed, and in only 3 were there more than 2 cases. In Copenhagen there were only 6 houses in which more than 1 case occurred. At Cologne, Copenhagen, Berlin, Boston, and New York the cases were distributed uniformly throughout, and there were no special centres of infection. The first patients observed by me at Paris in 1898 were scattered in as many different arrondissements and faubourgs as there were patients.

What, now, is the explanation of the comparative rarity of contagion in meningitis? We may assume with Leyden that the pathogenic agents are shut up in the cranial cavity and the spinal canal, and consequently cannot be spread abroad and become causes of the transmission of the disease. If, however, the pathogenic agents existed only in the meningeal exudate meningitis would never be transmissible. But in a certain number of cases these agents exist also in

the nasal mucus, pus from the ears, the expectorated matters, and in the urine, and so they may reach the external world and become the agents for the spread of the disease. It will therefore be useful to inquire under what circumstances the products of secretion or of excretion may contain the infectious agents of meningitis. Coryza is far from being constant in meningitis, and the suppurative inflammations of the tympanum, which are common enough in the disease, do not always result in perforation of the drum membrane.

It is not sufficient that these products of secretion contain the pathogenic agents of meningitis, but the germs must also preserve their virulence, and we know as a result of bacteriological examinations that this virulence is often very slight. We know that the activity of the pathogenic agents outside of the body is very readily destroyed by certain influences, such as heat, light, etc., which exercise a very rapid effect upon the germs of the disease. The fact that epidemics usually diminish or disappear in the warm season is doubtless due to the influence of these factors upon the virulence of the germs.

Another element which is to be taken into consideration in this study is the manner in which the pathogenic agents of meningitis enter the body, and also what influences facilitate or impede this entrance. Medin[106] has expressed the opinion that the contagious principle enters the cranium ordinarily by following the lymph spaces described by Axel Key and so passes through the fronto-ethmoid foramen or the cribriform plate of the ethmoid bone. The usual portal of infection therefore would be the nasal fossæ. Weigert had previously put forth this idea, supported by very solid arguments, in regard to tuberculous meningitis. Strümpell, Weichselbaum, and Netter have shown that inflammation of the nasal fossæ, of the accessory sinuses, and of the ears is encountered frequently in cerebrospinal meningitis, and this fact furnishes an argument in favor of the theory.

We must not generalize, however, for although coryza or angina has been observed at the beginning of a meningitis, the occurrence of such an inflammation is far from being constant. Silverskjold and Friis, who made an especially careful investigation in this regard, found these troubles almost always absent, and I also have noted that they were usually absent in the cases observed by me during the last epidemic. While admitting the possibility of direct nasal infection, I believe with Leichtenstern that the pathogenic agents most frequently reach the meninges by way of the blood, and that they enter this fluid from the pulmonary alveoli.

We have seen now that certain conditions favor the meningeal

localization; such are traumata, cerebral fatigue, and some organic lesion. Very often these occasional causes escape the most careful investigation, but their intervention is always necessary, and if the contagious character of cerebrospinal meningitis is not always evident it is perhaps in part because these occasional causes are wanting.

Our studies up to this time have shown us that meningitis is contagious, that its contagium separated from the body preserves its activity for an indefinite period, and may remain fixed on objects and in places, that it leaves the human body conveyed in the products of excretion, that it may penetrate by the nasal fossæ or by the pulmonary alveoli, that certain conditions favor or impair its vitality or its virulence, and that for the occurrence of meningitis the intervention of predisposing or occasional causes is often necessary. We shall return to a number of these points, but for the present we must see whether and in how far these various peculiarities correspond to the special properties of the microbic agents which bacteriology has led us to recognize in meningitis. We have seen that these agents are the pneumococcus and the capsulated diplococcus of Weichselbaum.

The pneumococcus is well known; it has been found in the expectoration and in the nasal mucus. Its vitality is of short duration in the ordinary culture media, but it resists desiccation a long time, as has been demonstrated by Foà and Uffreduzzi, Netter, Cassedebat, and Germano. I have shown that that it will live in the dust of hospital wards. Germano has shown that it can be transported by atmospheric currents. I have also shown that its virulence varies at different periods. The properties of the pneumococcus are precisely those which the pathogenic agent of meningitis ought to possess.

As to the diplococcus intracellularis of Weichselbaum, the relations of which to cerebrospinal meningitis are still to be determined, the documents are less numerous. However, we know that its vitality is usually very short, but that it may be longer under certain conditions. For example, the microbe has been found alive at the end of sixty days in gelatin tubes, and it resists desiccation for a long time. Germano[53] found its vitality preserved at the end of even ninety days. Finally Neisser[114] has shown directly that it is perfectly transportable by atmospheric currents, even the most feeble, and he concludes that it is very susceptible of aerial convection. The intracellular diplococcus therefore, like the pneumococcus, would appear to possess all the qualities necessary for the pathogenic agent of cerebrospinal meningitis.

The Question of Spontaneous Origin.

Another question in the solution of which bacteriology gives us great aid, is whether epidemic cerebrospinal meningitis can ever arise spontaneously. In the history of many epidemics it is impossible to discover the faintest indication of an importation of the contagium. If, however, we take into account the difficulties inherent in researches of this nature in large cities, the possibility of transmission of the disease by means of clothing and other objects, and especially the long vitality of the contagious principle of meningitis, we can readily see that we are not justified in all such cases in speaking of a spontaneous origin. The example given by Petersen,[140] who succeeded in tracing a connection between nearly all the cases occurring in Berlin during one epidemic, is in this respect very suggestive. Furthermore, bacteriology has shown us that the pneumococcus, the pathogenic agent most commonly in evidence in cerebrospinal meningitis, may be found in the buccopharyngeal cavity and the nasal fossæ of persons in health (Netter[119], [119a], [120]).

The intracellular diplococcus of meningitis has been less carefully studied to determine this point, but it has been found in the nasal fossæ of healthy persons by Heubner and Slawik.[66] If the pathogenic agents of meningitis may exist normally in the mouth and the nasal fossæ without provoking any symptoms, we are justified in assuming that under special conditions their virulence may become increased, and that then they may produce and transmit meningitis. I have shown that the degree of virulence may vary as regards the pneumococcus[121], [123], and also that when this virulence is greatest the pneumococci are most numerous. If now cases of meningitis, like those of pneumonia, are most frequent in the spring and during certain years, the reason is doubtless that at these times there are existent certain conditions favoring the virulence of the pneumococcus.

In 1888 I reported the case of a patient, with a psammoma passing through the cribriform plate of the ethmoid bone, who had a pneumococcal meningitis; and in 1890 the case of another patient who had a meningitis of the same nature following an attempt at suicide by shooting himself in the mouth with a pistol. In neither of these cases were the pneumococci carried by the tumor or the pistol ball, and before an entrance was opened for them they had existed in the nasal fossæ and the mouth. That which took place after gross lesions to favor the development of a sporadic meningitis, which meningitis might naturally have followed much less evident lesions, must necessarily intervene in the case of the occurrence of epidemic meningitis. Of this we have given some examples. What then remains to

separate sporadic from epidemic meningitis? Very little, since epidemic meningitis itself shows and can show its contagious character only under conditions relatively rare. Thus, as we have seen in the visitations in Boston, Cologne, and other places, epidemics of meningitis in a given locality are followed by cases of sporadic meningitis, and these cases again are followed after a variable interval by new epidemics of the disease. Furthermore, bacteriology shows us that the same microorganisms are present in sporadic and epidemic meningitis.

Relation between Pneumonia and Cerebrospinal Meningitis.

Certain writers have long been struck by the close relations existing between pneumonia and epidemic cerebrospinal meningitis. Among these authors we may mention especially Webber, Lewis Smith, Medin, Bozzolo, Netter, Runeberg, and Leichtenstern. The question is one to which we may devote a little attention. The arguments brought forward in support of a relation between these two affections are based on pathological anatomy, clinical history, etiology, epidemiology, and bacteriology. We will take them up in this order.

Pathological anatomy shows us that pneumonia frequently complicates epidemic cerebrospinal meningitis, and that suppurative meningitis is rather frequently found at autopsy in cases of pneumonia. In support of the first of these assertions we may cite Karg (who found pneumonia eighteen times in sixty cases of meningitis), Medin, several observers of the epidemic of 1863, and Bozzolo, Foà and Uffreduzzi, and Bonome in Italy.

Suppurative meningitis accompanying pneumonia has been the subject of still more numerous investigations and researches. This meningitis, which may be only an autopsical discovery not revealing itself by any symptoms during life, is a more or less frequent complication of pneumonia according to the locality and to the year. Immermann and Heller found it at Erlangen 9 times out of 30 autopsies made in 1866–68; these are the highest figures of any observer. Osler at Montreal noted it in 8 out of 93 autopsies, or in 7.76 per cent. Bozzolo at Turin and Milan, in 1868–82, found the lesions of meningitis 38 times out of 941 autopsies, or in 4.2 per cent., while Jürgensen at Tübingen found only 1 case in 72 autopsies, or 1.39 per cent. (Netter[xii]). From one hospital at Cologne Leichtenstern collected the following figures:

1879–84............	2 out	of 875	cases,	or	.23	per cent.
1885...............	0 "	" 244	"	"	0	" "
1886–87............	6 "	" 516	"	"	1.16	" "
1888–92............	1 "	" 765	"	"	.13	" "

I have demonstrated that these cases of meningitis complicating pneumonia occur usually in series.

Another argument from pathological anatomy, on which Bozzolo and myself have specially insisted, is that certain serous inflammations (pleurisy, pericarditis, endocarditis, peritonitis, and arthritis) frequently complicate both pneumonia and meningitis. Finally we are often struck by the almost identical characters of the fibrinopurulent exudate in the two diseases.

Among the symptoms common to both affections we may mention the following: the usually sudden onset peculiar to both pneumonia and meningitis, the common absence of any relation between the intensity of the local lesions and the general symptoms, and the great frequency of herpes in both diseases. Hæmatoscopic researches have shown that the two diseases are accompanied by a very notable increase in the proportion of white corpuscles.

A study of the etiological conditions shows us that meningitis, like pneumonia, attacks by preference persons of vigorous constitution who were in previous good health, and that both diseases are more common in winter and spring and less so in the summer and autumn. Both cold and traumatism may play the rôle of occasional causes in each of these diseases, although their action is apparent in only a very small number of cases.

A study of the epidemics of meningitis shows us that they have often coincided with a period of unusual frequency of pneumonia, the cases of the latter being so numerous as to warrant the appellation of an epidemic. We may mention here more particularly the reports of Gasc and of Comte[27] at the close of the wars of the Empire and those of the American physicians at the beginning of this century. The years 1885 and 1886, which were so fecund for the history of cerebrospinal meningitis, were also remarkable on account of the unusual frequency of pneumonia, and it is a curious detail that at this time there was some influence at work the effects of which were apparent in both hemispheres. This same coincidence was noted by me in Paris in 1886, by Foà and Uffreduzzi at Turin, Friis at Copenhagen, Leichtenstern at Cologne, and Runeberg at Helsingfors. At Copenhagen the number of cases of pneumonia between January 1st and July 31st, 1885, was 898, while in 1886 during the same period it was 1,241. At Helsingfors Runeberg gives the following as the number of deaths from pneumonia in the years 1882–87: in 1882, 313; 1883, 408; 1884, 303; 1885, 444; 1886, 594; 1887, 346. The years 1885 and 1886 were the years when meningitis prevailed epidemically. Finally in New York in 1872 cerebrospinal meningitis reached its acme between February 1st and June 1st, and

during these four months diseases of the respiratory passages, phthisis excepted, caused 1,707 deaths, while during the eight other months of this year the same affections gave a total of only 1,336 deaths.

We observe a still more close relation in cases in which, in the same group of individuals, we find at the same time some affected with pneumonia and others with cerebrospinal meningitis. Thus at Orléans, from January 30th to April 14th, 1886, there were in the two regiments of artillery fourteen cases of meningitis and twelve of pneumonia (Lemoine[94]). At Copenhagen in 1886 a packet boat called the *Daneborg* served as a guard boat for the sailors. During the spring there were forty men in this ship attacked by pneumonia and two by meningitis (Friis). At Montpellier from November, 1893, to January, 1894, Grasset[58] treated in his clinic seven soldiers from the same regiment, of whom two had cerebrospinal meningitis, one a meningitis following pneumonia, and four pneumonia or pulmonary congestion. Leichtenstern, in attendance upon a family in which there were four children, treated on February 25th a child with pneumonia complicated with meningitis which caused death at the end of thirty-six hours. On the 27th of the same month he treated another child suffering from cerebrospinal meningitis followed by hydrocephalus, which ended in death at the expiration of nine weeks. The head of the family had had in the same house an attack of classical pneumonia, from which he recovered.

We have reserved for the end the argument derived from bacteriology, which shows us that the pneumococcus is the most frequent pathogenic agent of cerebrospinal meningitis. Must we conclude with Medin[106] that pneumonia and meningitis are due to the same infectious agent, which in one case is localized in the lungs and in the other is arrested in the lymphatic vessels of the pia mater? The fact that pneumonia is ordinarily a sporadic affection while meningitis is usually observed in the form of epidemics need not detain us long. We have just shown, indeed, that no line of demarcation can be drawn between epidemic and sporadic cerebrospinal meningitis, and furthermore one has only to remember the numerous instances of pneumonia occurring in families, in certain houses, and in aggregations of troops, and indeed in even more extensive epidemics, to recognize the fact that it is not always sporadic. Epidemic cerebrospinal meningitis may break out apparently spontaneously, without any direct evidence of importation, just as does pneumonia, and the existence in health of the pneumococcus in the mouth and pharynx explains these cases of meningitis as well as those of pneumonia.

The close relation between pneumonia and cerebrospinal meningitis cannot, therefore, be doubted. We must, however, note two peculiarities which prevent us from concluding that the two diseases are absolutely identical, leaving aside for the moment those cases of meningitis in which a pathogenic agent other than the pneumococcus has been found.

The first of these facts is that pneumonia has not been common in all the epidemics of meningitis, and also that meningitis is by no means frequent in all epidemics of pneumonia. The second fact is that it is not exactly during the course of an epidemic of cerebrospinal meningitis that we observe the greatest number of cases of pneumonia complicated with meningitis, for a careful analysis of the facts shows us that such complications are more frequent before and after the epidemics of meningitis than during their course. The very interesting cases collected by Immermann and Heller were observed at the time that the epidemic of meningitis at Erlangen appeared to be at an end. From the data given by them we may construct the following table:

	Before the epidemic 1862–63.	After the epidemic 1866–67.
Autopsies in cases of pneumonia	8	22
Meningitis found at these autopsies	2	9
Percentage of cases of meningitis	25	40.9
Autopsies on cases of meningitis	5	3
Pneumonia found at these autopsies	2	1
Percentage of cases of pneumonia	40	33.3

The figures collected by Sievers[x1] at the clinic at Helsingfors were as follows:

	1880.	1881.	1882.	1883.	1884.	1885.	1886.
Pneumonia autopsies	6	6	10	11	3	13	15
Meningitis found	0	0	1	1	2	3	1

Of these seven years 1885 and 1886 were marked by epidemics of meningitis. But the proportion of cases of meningitis complicating pneumonia was greatest in the year 1884, while in the year 1886, during the epidemic, there was a lower percentage of complicating meningitis even than in 1882 or 1883.

The following are the statistics of the Milan General Hospital from 1868 to 1882, collected by Bozzolo:

	Autopsies on cases of pneumonia.	Meningitis complicating.	Percentage of meningitis.	Meningitis without pneumonia.
1868	58	1	1.88	2
1869	41	1	2.68	6
1870	55	1	1.85	3
1871	66	3	4.51	10
1872	47	3	6.38	6
1873	37	5	13.50	5
1874	69	5	7.24	9
1875	92	5	5.43	10
1876	78	2	2.56	1
1877	88	1	1.13	5
1878	105	7	6.66	1
1879	66	1	1.50	8
1880	47	3	6.38	2
1881	38	..	....	2
1882	50	..	....	1

From this we see that the year in which the proportion of cases of meningitis complicating pneumonia was greatest, that is 1873 (13.5), there were fewer cases of independent meningitis (five) than in the two following years in which there were nine and ten respectively. In the year 1879, in which the number of cases of uncomplicating meningitis was relatively high, the lesions of meningitis were found only once in sixty-six autopsies on the bodies of persons dying of pneumonia.

In 1898 at Paris there were numerous cases of pneumonia, but in my hospital wards I did not see a single case of pneumonia complicated by meningitis, although epidemic cerebrospinal meningitis was prevailing that year.

We shall close this section by a citation of the facts collected by Leichtenstern, which are the most exact and the most convincing of any. They were taken from his hospital service at Cologne. In the epidemic year 1885 there were 63 cases of meningitis and 244 of pneumonia, but there was not a single instance of the complication of one disease by the other: In the two following years there were still many cases of pneumonia, and the epidemic of meningitis continued, 24 cases being observed. During this period 6 cases of pneumonia, complicated by meningitis, occurred close together. From 1888 to 1892 pneumonia was less prevalent, 765 cases in all coming under observation, and there were very few cases of sporadic meningitis. Of these 765 cases of pneumonia only 1 was complicated by meningitis. Finally, from February to June, 1893, there were again many cases of pneumonia at Cologne, and during this time Leichtenstern observed 7 cases of cerebrospinal meningitis. Of these cases, in 2 the meningitis was uncomplicated; in 2 meningitis and pneumonia

appeared simultaneously; in 2 the meningitis preceded the pneumonia by four and two days; in 1 the pneumonia appeared first and the meningitis developed on the sixth day. Leichtenstern, after studying his personal cases with great care, suggests that possibly the pneumococcus may become transformed into a variety capable of causing meningitis, and that after this transformation has occurred and the variety has become well individualized it can then give rise only to meningitis; but before its complete individualization it may cause both pneumonia and meningitis. He explains in this way how at the height of an epidemic meningitis is not complicated by pneumonia, and how, on the other hand, this complication is common at the beginning and at the end of an epidemic of cerebrospinal meningitis. We have just seen that the facts cited by Leichtenstern are not isolated ones, and that similar instances have been observed at Erlangen, Helsingfors, and Milan.

The bacteriological investigations of Foà, Banti, Bonome, Kruse, and Pansini have shown the existence of varieties of the pneumococcus, capable of being brought back to the original type, yet sufficiently differentiated. I have noted similar differences and have shown that the microbe usually found during the epidemic of 1898 at Paris had the characters which Bonome[15] attributes to his streptococcus capsulatus, which is rounded rather than lanceolate, and is less pathogenic for mice. But the pneumococcus found in cases of meningitis complicating pneumonia is ordinarily especially virulent and is distinctly lanceolate in shape. One can readily see how these facts coincide with Leichtenstern's hypothesis.

In establishing the fact in 1887 that certain epidemics of cerebrospinal meningitis were incontestably caused by the pneumococcus, I raised a question whether this microbe was always the cause of meningitis, or whether other pathogenic agents might not be at fault in other epidemics (Netter[xii]). A certain number of observers have apparently confirmed this view by demonstrating, alongside of the pneumococcus, the influence of another pathogenic agent, the diplococcus intracellularis meningitidis. I see no good reason for believing that this may not also be an active cause in certain epidemics. But none of the attempts which have been made to differentiate the epidemics due to Weichselbaum's diplococcus from those due to the pneumococcus has been attended with any success. Wentworth[176] says that the pneumococcal meningitis is always fatal in contradistinction to that caused by the action of the diplococcus. As early as 1887, however, I demonstrated that its curability was one of the most evident characteristics of the pneumococcal meningitis. I have

shown in the section on bacteriology that relations, of which we do not yet know the exact importance, exist between the pneumococcus and the diplococcus intracellularis.

Prophylaxis.

Whatever opinion we may entertain concerning the frequency of contagion as an agent in the spread of meningitis, it is nevertheless useful to take certain precautions in case of the occurrence of this disease, similar to those which we observe in the presence of acknowledged infectious diseases.

In November, 1888, the Prussian Government prescribed certain regulations, to which we give a ready assent and approval. These were: obligatory notification, isolations of the sick, disinfection of the sick-room and of the patient's linen, outer clothing, and other effects, especially the handkerchiefs used by him. It is because these measures were not taken or were carried out in an inefficient manner that meningitis persisted in the barracks of the French army and among the regiments, even after their removal to new barracks.

The methods of disinfection as well as the disinfectants to be employed are precisely the same as those counselled in the case of other infectious diseases.

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DYSENTERY.

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DYSENTERY.

Definition.—Dysentery may be defined as an infecto-contagious disease, endemic in warm countries, sporadic or epidemic in temperate regions, characterized anatomically by lesions of various organs, such as specific ulcerations of the large intestine, and clinically by the occurrence of frequent bloody, mucous, or serous dejections, accompanied by tormina and tenesmus, and by more or less accentuated general symptoms.

Introduction.

Dysentery, a disease endemic in some parts of the world and liable to extend epidemically to others, by its frequency, the extension of its geographical dominion, its rapid expansion, the excessive gravity of its epidemic onslaughts, and its character of a complaint developing during great famines and accompanying armies on the march, is undoubtedly one of the most important diseases in the nosological table, and its study deserves the greatest attention and care.

Notwithstanding modern investigations on the etiology and pathological anatomy of dysentery, authors have not yet been able entirely to agree. Some describe various affections under this head; others deny its contagiousness and specificity; others, from the ubiquitous character of dysentery, infer that there is no etiological unity.

Authors in general, treating of the subject, allow themselves to be guided now by preconceived ideas, now by a limited clinical observation. Nevertheless, for us to form an exact opinion on dysentery, it is necessary to see it in its endemic foci, to observe it during its epidemic attacks, to discover what are its means of dissemination and propagation, to find out why it attacks certain localities, sparing others subject to the same conditions of climate, why in a given neighborhood it strikes certain individuals, passing over others, etc. For these reasons physicians who observe the disease in the tropics find themselves in the most favorable condition to form an exact opinion on it, and indeed from them have come the best contributions published on dysentery.

History.

Dysentery has been known from the most remote antiquity, and belongs to all ages of history and to every inhabited region on the globe.

It was observed by Hippocrates, mentioned by Herodotus, admirably described by Aretæus and Celsus, and has occupied the attention of practitioners of all times. If we consult the epidemic nomenclatures of Hirsch and Haeser, we shall see it figure among the widespread diseases of antiquity and the Middle Ages, we shall follow it in its devastations from century to century, now presenting itself epidemically in different countries and cities, now following armies on the march, now developing among sufferers from famine.

History also tells us that dysentery was not invariably considered as a scourge, and did not always assume a grave and malignant character; in many localities it appeared as a more or less benign disease of the warm season.

It would be tedious to follow the history of dysentery from the Hippocratic epoch down to our days. It is worth while, however, to call attention to the idea that the physicians of antiquity had concerning this disease, to signalize the opinions held by physicians of the eighteenth century, and compare them with those that held sway during the first half of this century. This comparative study is full of instruction, and proves once more that in medicine conceptions based on the rigorous and exact observation of facts resist, and will always resist, the powerful influence of doctrines and systems which have succeeded each other in the course of time.

Aretæus gives us a good description of the symptoms of dysentery. According to him the disease is due to the ulceration of the intestines. The ulcers may be small and superficial, in which case they are relatively harmless; they may be deeper and more dangerous; finally they may assume a phagedenic and gangrenous character leading to a fatal termination. When chronic, the edges of the ulcers are thick, rough, unequal, indurated, and difficult to heal over; after healing they sometimes open anew. The causes of dysentery, he says, are various—such as indigestion, continual cold, deteriorated food, exposure to cold and cold drinks.

Galen admits two kinds of dysentery: one coming from disease of the liver, or hepatic dysentery, and the other resulting from ulceration of the mucous membrane of the intestines. Cœlius Aurelianus defined dysentery as *rheumatismus intestinorum cum ulcere.* Celsus condenses the clinical and anatomical history of the disease in a suc-

cinct description, the principal features of which may still be accepted at the present day. "Intus intestina exulcerantur: ex hic cruor manat, isque modo cum stercore, aliquo semper liquido, modo cum quibusdam quasi mucosis exernitur; interdum simul quædam carnosa descendunt; frequens dejiciendi cupiditas, dolorque in ano est; cum eodem dolore exiguum aliquid emittitur, atque eo quoque tormentum intenditur."

The clear and exact conception of dysentery in the works of ancient authors was modified in the course of time under the influence of the ruling medical doctrines. The morbid unity so well established disappeared and was replaced by the varied forms of dysentery, described and considered as different entities without the common features of clinical and anatomical characters. The disease came to be confounded with simple diarrhœa and enteritis.

Sydenham did not give much attention to intestinal lesions, and it is possible that he and his disciples mistook other diseases for dysentery. In compensation, however, he gave it the clinical specificity that it had lost in the course of centuries, considering it a general disease, a morbid entity distinct from symptomatic diarrhœa, a fever thrown on the intestines. He describes three forms: the first characterized by gripes without stools, or dry colics accompanied sometimes with fever; in the second there are frequent slimy motions, attended with griping and usually with fever, which, he says, is a true bloody flux or dysentery, although there may be no passage of blood from first to last; in the third, along with fever there are frequent bloody and mucous stools, with griping and tenesmus.

During the Seven Years' War dysentery developed concomitantly with malaria and typhoid fever, and by some observers was confounded with those diseases; they attributed to it features and symptoms entirely foreign to it, and made these last-mentioned diseases responsible for the grave phenomena and the great mortality. The admirable clinical descriptions of Degner, Pringle, and Zimmermann argued against this opinion. From these descriptions are to be inferred the great and rapid extension of epidemics, their considerable mortality, the sudden and truly malignant gravity of certain cases, and, lastly, the contagiousness of the disease.

According to Pringle dysentery is a pestilential disease; it is the expression of the putrid decomposition of the blood and humors under the influence of atmospheric vicissitudes, army fatigue, putrid miasmata, or contagion. It is always identical with itself, not presenting different forms. The same dysentery that he observed during the war of the succession in Austria he found afterwards in Scotland. Zimmermann observed in 1765, in the canton of Berne and in

the landgraviate of Thurgau, local epidemics which seemed to originate from the great epidemic propagated by the troops during the Seven Years' War. According to him, dysentery was of a bilious or putrid nature. Its constant association with putrid fever then prevailing, and certain analogies in its course, symptoms, and treatment seemed to demonstrate the fact. Being an extreme advocate of the doctrine of humors, he taught that the putrid principle, the internal and immediate cause of the fever, resides in the depravation of the bile, the most corruptible of our humors. He recognized two clinical forms: the putrid-bilious and the malignant. In this latter form the malignity is not a character inherent to dysentery; it rather results from foreign complications, true morbid associations (Kelsch and Kiener). Stoll, although an adept also of the doctrine of humors, formulated a very different conception concerning dysentery. He observed it as a sporadic disease, or in small seasonal epidemics. "It is a rheumatic fever," he said, "acknowledging the same material cause as that of rheumatism, that is, a serous matter, the humor of perspiration driven inwards by cold." He never saw the disease develop except in persons exposed to cold when overheated. As to the contagiousness, Stoll absolutely denied it. Hunter, who observed the disease in Jamaica in sporadic cases, did not consider it to be of an infectious nature or capable of transmission by contagion; he rather believed it to be a local affection, caused by the use of impure water, or the consequence of remittent fever. He gave a good description of the symptoms of the disease. The pathological lesions of dysentery, its anatomical characterization, so marked in the works of ancient authors, did not secure the attention of the physicians of the eighteenth century. After the writings of Sydenham, Willis, and Stoll dysentery was considered as independent of any intestinal lesion; what prevailed was catarrh, a purely functional modification. Zimmermann says that inflammation of the intestines is rarely met with; and Pringle himself, who in the first autopsies published refers to the existence of ulcer and gangrene, retracts later on, confessing that he mistook the facts observed.

But if the anatomicopathological lesions were relegated to a second place by the physicians of the eighteenth century, the same did not happen in relation to the clinical part and the nature of the disease, which were carefully studied by them. Two complete and minute descriptions are found in their works, leading to two different and opposite conceptions of dysentery. In the first it is considered a local disease of a fluxionary nature and not contagious; in the second it is a general disease of a putrid nature transmitted by contagion. The first referred to sporadic dysentery and that which is a seasonal

disease in temperate climates; the second to the epidemic dysentery of armies on the march. The description of this last received the sanction of Cullen, who in his Nosography defines dysentery as pyrexia contagiosa; dejectiones frequentes, mucosæ, vel sanguinolentæ, retentis plerumque fæcibus alvinis, tormina, tenesmus.

At the beginning of this century, when the doctrines of Broussais held sway, the notion of the clinical and etiological problems raised by the history of dysentery was abandoned, and the disease was regarded as a phlegmasia of the large intestine, characterized by different degrees of intensity. Cruveilhier considered dysentery to be a phlegmasia localized in the rectum and provoking tenesmus; he denied its specificity, however, and thought it might be one of the modes of termination of the majority of chronic diseases. Andral regarded as scales of concrete mucus the fragments of mucous membrane expelled by the evacuations. Chomel denied all the process of ulceration, whether generalized over the mucous membrane or localized in the glands, and asserted that the authors of antiquity were erroneously led to admit the existence of ulcerations by reason of the presence of blood in the dejections. According to Virchow, dysentery is a clinical syndrome, corresponding anatomically to a simple catarrh or to a diphtheritic affection; as a rule, dysentery commences by a catarrh and only becomes diphtheritic under the influence of local causes, such as the contact of hardened fecal matter.

These ideas concerning the dysenteric process prevailed during nearly the whole of the first half of the present century. Trousseau was, perhaps, the only author who remained faithful to tradition. He established the correctness of the ancient description, referring frequently to intestinal ulcerations, and recognizing in epidemic dysentery four clinical forms—the inflammatory, the rheumatic, the bilious, and the putrid.

The reaction against the prevailing ideas began with the works of the physicians who studied the regional epidemics of France—Gely, Thomas, Masselot, and Collin; it was completed with the studies and investigations effected in Algeria and in British India. Thomas, who observed dysentery in Tours (France), writes: "I recognized, after having carefully performed a considerable number of autopsies, that the opinions of the ancients were very correct, while those of the moderns are entirely wrong." Further on he adds: "The mucous membrane is promptly invaded by numerous ulcerations, so well characterized and so constant that I admit as an undeniable fact that the ulceration of the mucous membrane is an essential character in dysentery, just as the phlyctenas are an essential character in erysipelas, the core in a furuncle, and pus in the phlegmasia of the cellular tissue."

An endemic disease in tropical regions where, besides the special gravity of its acute manifestations, it exhibits a marked tendency to become chronic, dysentery has always constituted a favorite subject of observation and study with physicians practising in these parts. In the "Pathology" of Annesley, the eminent English physician, whose work performed in British India marks an epoch in the history of intertropical pathology, dysentery figures as a disease of a bilious nature, originating almost always in the combined action of various causes. "Very frequently, in addition to the predisposition arising from plethora, fatigue, or a loaded state of the large bowel, and a deranged condition of the alvine secretions, several of the common exciting causes of the disease, such as intoxications, exposure to the night air, wearing wet or damp clothes, insufficient clothing, sleeping on the ground, and unwholesome food, act in conjunction." When the functional disturbance created by these causes interests more particularly the bilious secretions and determines a modification in the quantity and quality of the bile, the latter, accumulating in its excreting conduits or flowing into the digestive tube, provokes sometimes the profound disorders of suppurative hepatitis, and sometimes the appearance of dysenteric flux. Thus the practitioners of India did not fail to remark the intimate relation existing between dysentery and so-called tropical abscess of the liver. Differing from contemporary European observers, Annesley recognized the supreme importance of intestinal lesions, not only in the simple forms of the disease, but in those attended with accentuated hepatic disorders. He gave a good description not only of the symptoms of dysentery, but of the lesions found in the intestine and other viscera. So far as regards contagion, Annesley admits it, not as a constant and invariable character, but as being possible under certain rare circumstances.

The opinions of Annesley prevailed among the physicians of India and other English colonies from the beginning of the present century to a period very near our own days, being modified only by the pathological studies of Bayle, Parks, and Aitken. These last-mentioned observers insisted on the specificity of the dysenteric process, establishing the ulcerous character of the intestinal lesions.

In Algeria, Senegal, and the Antilles, the French physicians soon emancipated themselves from the ideas that still obtained in Europe, and described the specific lesions of dysentery, insisting on the presence of ulcerations and false membranes, and admitting that the lesions begin at the apex of the follicules. In this particular the works of Haspel, Canteloup, and Cambay are conspicuous. Dutrouleau went further and established the gangrenous character of tropical

dysentery. According to him, in the sporadic or epidemic dysentery of temperate regions may be found various lesions, presenting variable degrees and characters, according to the characters presented by the disease during life; but in the endemic dysentery of warm countries, we find only one anatomical character, which is always the same, varying only in intensity or extension. This character is gangrene—gangrenous scab, ulceration. Dutrouleau says: "Ulceration is indeed the anatomical character of endemic dysentery, and this ulceration is the result of the removal of a scab determined by gangrenous inflammation; it characterizes the disease anatomically, just as the ulceration resulting from the destruction of Peyer's patches characterizes typhoid fever."

The descriptions of Dutrouleau and his predecessors were completed by Heubner, Cornil, and chiefly by Kelsch and Kiener, from whose works I shall have to borrow largely when I treat of the subject in detail further on.

The French authors of the first half of this century, though well informed so far as regards the anatomical evolution of the dysenteric process, lost themselves in conjectures, which were sometimes extravagant, when they attempted to solve the etiological problem. Dysentery was by them alternately considered as liable to develop as the result of a cold or an irregularity in diet, or under the influence of trifling causes, as resulting from the action of meteorological elements, and as a particular manifestation of malaria. This last opinion, maintained for a long time by the physicians of Algeria, and, among the English by Aitken, exerted a marked influence in Brazil, where, until a very few years ago, it prevailed, owing to the frank support of the great Brazilian physicians Torres Homem, Barão of Petropolis and Barão of Lavradio. It was the French physicians themselves, and, among them, Dutrouleau and Felix Jacquot, who contributed most to overthrow it, showing that dysentery and malaria differ widely in their geographical, epidemiological, anatomical, and clinical characters.

The microbic conception of infectious diseases greatly facilitated the solution of the etiological problem of dysentery. Numerous investigators working in countries situated in the most diverse latitudes have studied with particular care the microorganisms found in individuals suffering from this disease, and, notwithstanding experiments and opinions to the contrary, the discovery of Losch and Kartulis of the living cause of dysentery continues to gain acceptance, being confirmed by the majority of modern observers. On the other hand, the data which science registers to-day in relation to the secondary causes of the disease, and to the manner in which it origi-

nates and is propagated in and outside of endemic centres are of a nature to establish the specificity and unity of dysentery.

Councilman and Lafleur, two careful and competent American observers, who published an excellent monograph full of original investigations on the etiology and pathological anatomy of dysentery, endeavored to establish a distinction which I do not think entirely convenient, and which appears destitute of foundation. They hold that the term dysentery embraces various affections of the intestines, and describe a special form, which they call "amœbic dysentery." "Amœbic dysentery," they write, "is a form of dysentery which, etiologically, clinically, and anatomically, should be regarded as a distinct disease. Clinically, the disease is characterized by the presence of amœbæ in the stools, which in addition present physical characters different from those seen in the stools of other forms of dysentery. Anatomically the disease is characterized by the production of ulcers in the colon, which generally differ from those found in any other form of dysentery. The ulceration is produced by infiltration of the submucous tissue and necrosis of the overlying mucous membrane, the ulcer in consequence having the undermined form. Frequently, in addition to the ulcers, there is infiltration of the submucous tissue without ulceration. Abscess of the liver is a frequent complication, much more so than in any other form of dysentery." And they conclude with the assertion that "this is the form of dysentery which has been commonly called tropical dysentery."

At first sight, we might suppose that Councilman and Lafleur considered the dysentery of the tropics as different from the dysentery observed in temperate regions; such is not the case, however, since these observers made their investigations far away from the tropics and write, referring to amœbic dysentery: "The disease is widely distributed in most countries in Europe, in most parts of the United States, and in the tropics everywhere."

It would have been more logical and rational had Councilman and Lafleur, while establishing the relation of cause and effect between dysentery and the amœba coli, proclaimed the specificity and unity of the disease, separating it from all forms of enteritis not proceeding from the same cause. To admit a dichotomy in the morbid process, to recognize the existence of an amœbic dysentery and another not amœbic seems to me absolutely unacceptable. Dysentery is one and one only, whether it be considered from an etiological, clinical, or anatomical point of view. Various etiological factors, some of which are trifling even, concur efficaciously to the genesis of dysentery; they act in a secondary manner, preparing the ground and aiding the action of the dysenteric germ, without the concourse of which the

disease cannot occur, whatever be the latitude in which the observation is made. Various clinical modalities, from mild dysentery to gangrenous dysentery, are observed, and sometimes simulate different diseases; nevertheless, among these varied clinical features common traits are always found, which represent the clinical character of the disease. The same may be said in regard to the pathological anatomy; various anatomical forms have been described, but among the lesions of different character, extension, and seat, we always find a characteristic lesion, which represents the true anatomicopathological substratum of the disease. Just as it is not allowable to separate acute miliary tuberculosis, pneumonic tuberculosis, and chronic ulcerous tuberculosis as constituting three special diseases; just as we may not consider atrophic beriberi and dropsical beriberi as two distinct diseases, although appearances may lead us to do so, in like manner there is nothing to justify the division of dysentery into two or more different affections from an etiological, anatomical, and clinical point of view. Dysentery is one disease and one only, and is always the same whether observed in the tropics as endemic and with marked tendency to become chronic, or in temperate regions as sporadic or epidemic.

Geographical Distribution.

It is difficult to establish the geographical dominion of dysentery by means of fixed parallels. A truly ubiquitous disease, it is not limited by latitudes, and we think we can affirm without fear of denial that there is no country and no extensive district in any country, from the equator to the poles, in which dysentery has not been observed in the sporadic, endemic, or epidemic form. In Greenland, northern Russia, Norway, Iceland, Sweden, Siberia, etc., its presence has been noticed at different times. According to Lombard it is one of the most widely spread diseases in Sweden, where it sometimes assumes great gravity; in the year 1857, for example, 37,000 persons were attacked with it in that country, of whom 10,000 died. Every country in Europe has paid a heavy tribute to dysentery; more or less extensive and deadly epidemics have at different times, generally at somewhat long intervals, devastated these countries, producing ravages similar to those of the so-called "pestilential diseases." *Morbus post pestem maxime timendus*, said Frank, referring to dysentery. Besides these great epidemics spreading over numerous districts of the same country, passing from one country to another and sometimes assuming the character of real pandemics, dysentery has been observed in the temperate zones under the form of regional epidemics, that is, small epidemics, frankly depending on the seasons,

and limited to a village, a plantation, or a community. Mild sporadic cases of short duration are observed during the hot summers in all countries of the temperate zone.

As we approach the tropics dysentery becomes more and more frequent, and its annual reign lasts longer. It gradually loses its character of a seasonal disease to become permanent. In intertropical and subtropical regions it is endemic, and presents a marked tendency to become chronic. In the endemic centres themselves or outside of them, it often presents itself under the form of more or less extensive and grave epidemics.

The endemial zone of dysentery may be said to be limited on the north by 40° of latitude N., and embraces, in Europe, the southern provinces of Spain, Sardinia, Calabria, Sicily, Greece, and adjacent islands; in Asia, Asiatic Turkey, Syria and Mesopotamia, Persia, Afghanistan, Beluchistan, Hindostan, Farther India, the Philippine Islands, Japan, and the South of China. In Africa, Morocco, Algeria, Tunis, Tripoli, Egypt, Arabia, Senegambia, and Abyssinia. In America, the United States in all the regions situated to the south of the States of Virginia, Kentucky, Missouri, Kansas, and Colorado; Mexico, Central America, West Indies, Colombia, Venezuela, and the Guianas. To the south the endemial zone of dysentery is limited by 35° of latitude S., comprising, in Africa, all the countries situated to the south as far as Cape Colony. In South America, part of the Argentine Republic, Chili, Peru, Bolivia, Uruguay, Paraguay, Equador, and Brazil. In Oceanica, Java, Sumatra, Borneo, New Guinea, Australia, and the Feejee, Hawaiian, Marianna, Marquesas, and Tahiti Islands.

In all these different countries dysentery is not equally frequent, nor do its endemial foci embrace all the extension of territory belonging to them; not infrequently it is observed even in localities heretofore immune, situated very near to others which are intense endemic foci. Ordinarily dysentery is the more frequent and permanent the nearer it is to the equator. This rule, however, is open to exceptions; there are regions lying on the equator, such as the states of Pará and Amazonas in Brazil, Peru, etc., where the disease, although frequent, is much less so than in other places situated far from the equator, as Japan, for instance. In this last country, according to Dr. Kiyoski Shiga, dysentery prevails annually with considerable intensity; from June to December, 1897, 90,000 persons were taken with it, 20,000 of whom died. In Brazil dysentery is observed all over the country, from the states of Pará and Amazonas at the extreme north to the state of Rio Grande at the extreme south. It prevails as an endemic of weak intensity during all the year, increas-

ing with more or less violence in summer; some years, however, the disease acquires here and there an epidemic character, when it spreads from one locality to another, invading places previously spared and developing independently of the influence of the seasons. It has never produced ravages comparable to those of yellow fever or cholera; the Brazilian epidemics have never shown extension and malignity equal to those of certain European, Asiatic, or African epidemics. Even the epidemic observed during the drought and consequent famine in the state of Ceará in 1879 was relatively small. The greatest epidemic in Brazil of which we have any knowledge was that which began in the city of Rio de Janeiro, in October, 1863, and lasted until the end of 1865, spreading to the states of Rio de Janeiro, S. Paulo, and Minas; and notwithstanding its great duration and the vast zone attacked, this epidemic did not cause three thousand deaths.

Etiology.

Clinical observation, while confirming in a great measure the opinions emitted by ancient physicians, shows that dysentery may appear and develop under three widely different conditions: as a disease of the seasons in temperate climates, constituting local epidemics, not much inclined to spread and not very fatal; endemic in hot climates with marked tendency to become chronic; epidemic at certain times and in all latitudes, possessing great power of dissemination and high mortality, assuming then the character of a pestilential disease.

Different causes have been invoked to explain the origin of these modalities of dysentery, considered for a long time as distinct morbid entities. Under this last aspect the etiology was much simplified; to each one of the so-called morbid species corresponded a special order of causes, and the etiological diversity justified the difference of the nature of the disease and the different conditions under which it develops. A meteorological influence would determine the breaking out of dysentery in local epidemics of temperate climates; the endemic dysentery of the tropics would be due to the combined action of the heat and of the miasma of swamps, in the opinion of most observers; army dysentery would have a complex etiology—sudden exposure to cold (the English army on the evening of the battle of Dettingen, during the Seven Years' War; a French expedition column crossing a river in Africa, etc.); the eating of bad and spoiled food; the use of stagnant and marshy water, etc.; finally, the dysentery of famine-stricken districts would be owing to want, to hunger, and to the eating of irritating substances not fit for food.

It was found, however, that the dysentery of temperate and cold climates might sometimes lose the character of a seasonal disease, and further, that a local epidemic might become the starting-point of a widespread epidemic, the disease invading the neighboring localities and districts, ravaging a whole country, and exhibiting entire independence of meteorological influences. Cheyne saw dysentery begin in Ireland in the summer and last all through the autumn and winter, only terminating in the spring. In Siberia, the dysentery that spread over the country in 1732 produced ravages as late as January, notwithstanding the excessive severity of the winter. The epidemic that broke out in 1852 in Sweden, and killed thousands of persons, had at first a local character; the disease began in a few isolated districts, within a limited area, and gradually advanced over the country during successive years. It was also found that in warm climates dysentery develops and prevails in certain localities, sparing others situated on the same isothermal line, under identical conditions of climate, and that the endemic foci of dysentery and of malaria do not correspond precisely. The former disease is not observed in some localities annually visited by the latter, and it prevails in other places, as, for instance, the island of Réunion, exempt from malaria. At Grande Terre, on the island of Guadeloupe, malaria prevails with intensity, and dysentery is only exceptionally seen, while at Basse Terre, on the same island, dysentery is intense and wide-spread and malarial fevers are rare. Madras is the presidency in India that most suffers from dysentery, and it is also that which is least victimized by malaria. Finally, it has been found and demonstrated that atmospheric vicissitudes, irregularities in diet, bad food, and hunger are not capable in themselves of causing dysentery.

Anatomical investigations in Europe, in India, in Africa, and in America have shown that dysentery is always the same in whatever latitude it is observed. Clinical medicine in its turn, and also therapeutics confirm the unity of dysentery in all climates, showing that the small differences observed are due to secondary circumstances. But if the disease may be observed from the poles to the equator; if it is found in all climates, in ordinarily healthful places, as well as in others where malaria prevails; if it attacks not only persons exposed to atmospheric vicissitudes, but also those who keep themselves protected and sheltered; if it does not spare rich or poor, and attacks those starving with hunger and those who fare sumptuously, those who indulge excessively in alcoholic drinks and those who abstain from the use of alcohol, the inhabitants of cities provided with pure water, and those who in the country use stagnant water, etc., then it is clear that atmospheric changes,

exposure to cold, irregularities in diet, the use of impure water, hunger, malaria, etc., cannot be considered as determining causes of dysentery.

Some authors, and among them Léon Colin, think that none of these etiological factors can be considered as the efficient cause of the disease to the exclusion of the others, but they admit the plurality of causes. "If dysentery," writes L. Colin, "is liable to appear in so many places and circumstances, this ubiquity is a consequence of its etiological triviality; instead of being determined by one single morbid agent, as a virus attacking all the organism before producing the lesion, it may be provoked by all the causes of irritation of the large intestine." This opinion, which is contrary to the specificity of dysentery, cannot be defended. How are we to admit that trivial causes, acting constantly on large communities, can generate a disease so capricious in its appearance, in its epidemic evolution, and in its endemic paroxysms?

A careful etiological study shows that dysentery, in whatever latitude it be observed, is always due to the action of the same determining cause, that it starts and is propagated always under the influence of infection and contagion, and that it should be included in the group of parasitic diseases.

Infection.—Dutrouleau laid great stress on the infectious character of dysentery, demonstrating the geographical distinction between its foci and those of malaria. According to him the essential cause of the disease lies neither in meteorology nor in defective individual hygiene, but depends on special hydrotelluric conditions inherent to the localities. In the tropics the infectious character of dysentery is manifest, and nothing but this infectious character could explain satisfactorily the endemic nature of the disease and its predilection for certain districts of a country while sparing others in the same conditions of climate. In Brazil, for instance, dysentery is not observed in a uniform and continuous manner throughout the country; it has its favorite foci, and spreads from one place to another. In the city of Rio de Janeiro, sporadic cases of dysentery are observed all the year round; every summer, however, an epidemic breaks out, limited to one point of the city—the lunatic asylum; it attacks there a great many persons, and disappears at the end of the summer, without appearing in an epidemic character in the city proper; no similar fact is observed in other collective dwellings in the city—asylums, prisons, barracks, colleges, etc.

The predilection which the disease manifests for certain cantons, departments, and territorial districts in Europe, in which epidemics are observed with great frequency and sometimes with annual regu-

larity, argues in favor of its infectious and telluric character. Some departments in Brittany, France, have become notorious in this respect. Medical literature registers many cases showing the influence exerted by a contaminated and infected soil on the genesis of epidemics of dysentery. Czernicki relates that two French squadrons, the sanitary condition of which was as good as could be desired, occupied, towards the end of August, 1875, the Vadeney plantation, on the field of Châlons; dysentery broke out on the 1st of September, and only after the outbreak of the epidemic was it discovered that on the same ground there had encamped previously a regiment of cavalry, in which there had been numerous cases of dysentery. The epidemic disappeared as soon as the squadrons broke camp and abandoned the proximity of the focus of infection. In 1890, dysentery developed almost exclusively in a fraction of the troops assembled on the field of Châlons, and it was found that this fraction occupied exactly the region where the regiments attacked by the disease had encamped the year before. Trousseau relates that at Tours there are two barracks placed in the same relative position at an equal distance from the two rivers which traverse the city, one in the eastern suburb, the other in the western; the same hygienic regulations are adopted for both of them; in both of them the *régime* of the soldiers is exactly the same. Nevertheless, during thirty years, epidemics of dysentery have succeeded each other, having always for a starting-point the cavalry barracks, the infantry soldiers being attacked by the disease only in the hospitals when under treatment there for other affections. Kelsch and Kiener relate that dysentery raged for two successive years at La Rochelle, and was exclusively restricted to the Twenty-first and Thirty-fourth regiments of artillery occupying a locality impregnated daily and for several years by human and animal dejecta spread over the surface.

The influence of polluted soil did not escape the notice of the physicians of the eighteenth century. Pringle relates that, after the battle of Dettingen, the allied troops marched to Hanau, where they encamped; here dysentery developed in the soldiers with great intensity; as soon, however, as the army broke camp and left Hanau, the disease diminished to a marked degree and, shortly after the passage of the Rhine, disappeared entirely. Kelsch and Kiener record numerous instances in which outbreaks of dysentery appear to have been caused by the drying up of lakes and ponds, and the exposure of the slime and mud to the action of the sun. In the latter part of 1863, dysentery developed in the city of Rio de Janeiro with an epidemic character; it immediately acquired relatively great expansion, spreading throughout the city and suburbs, and extending also to the neighboring states. The outbreak of this epidemic coincided with the great excavations

made in all the streets of the city by the City Improvements Company, in order to lay the net of sewage pipes.

The facts quoted, besides many other similar ones to be found in medical literature and which I omit for the sake of brevity, prove that the producing cause of dysentery often lies in the soil in circumscribed foci of infection. These foci, which are best defined in cold and temperate climates, are represented by marshes and bogs which receive the drainage from dung-heaps and water closets, or by a soil impregnated with human dejections. In the tropics it is very difficult to limit these foci; according to Dutrouleau, irregular and high ground crossed by running water seems to be everywhere its favorite field. We cannot admit with Dutrouleau as the cause of dysentery a special miasm, exhaled from the soil and seconded in its effects by the heat of the climate. Neither can we admit that the disease is caused by the decomposition of organic matter accumulated in the above-mentioned foci; everywhere are found puddles, bogs, water-closets, dunghills, muck-heaps, etc.; and, nevertheless, dysentery appears only at certain periods and in certain places. Everything leads us to believe that those foci of infection originate the disease because they contain the producing agent of it, which finds in them a favorable medium for its existence.

Contagion.—The specificity of the agent causing dysentery is made evident by the property that the disease has of being transmitted by contagion. Many modern authors of reputation deny emphatically the contagious character of dysentery; others, following the opinion of Annesley, admit it only in special and very rare conditions. J. Rochard says he would never consider contagious a disease which, in order to develop in an individual in hot climates, required but a night's exposure to the open air without proper clothing. To this original opinion we may object that, in the north of Brazil, sleeping in the open air in a hammock is a common practice in the backwoods, and dysentery has never been known to originate from this cause. Arnould writes: "The contagion of dysentery is an illusion which is lost after a close observation in hospitals where patients with dysentery are received." There are on record hundreds of cases of dysentery contracted in hospitals, where there were dysenteric patients, by patients who entered with some other disease, and by nurses, pharmacists, and physicians. Corre admits the transmissibility of the disease, but he adds that this transmissibility is not contagion, because it is not effected by the immediate regeneration of a definite principle capable of inoculation. F. Roux and L. Colin are opposed to the theory of contagion and think that any cause capable of irritating the intestines can produce the disease. Bérenger-Féraud says that the immense ma-

jority of facts seem to prove that dysentery is not always contagious. Davidson writes: "Much of what we call dysentery is infectious in its nature. In some instances it appears to be contagious, but a closer observation of its mode of propagation in hospitals may show that the dysenteric discharges only become infective after they have undergone some changes outside the body."

The contagious character of dysentery is, nevertheless, perfectly demonstrated by an infinite number of facts recorded in medical literature since the last century. Referring to an epidemic in 1736, Degner declares that contagion was its principal cause; the disease broke out after the arrival of an infected person and spread from house to house, from street to street, from the city to the country and the neighboring cities. The English soldiers who contracted dysentery in the field of Hanau were transferred to the hospital of Feckenheim; there the disease assumed a seriously infectious character, spreading to a great number of individuals employed in the service of the hospital, and then extending to the population of the city. Pringle recapitulates his observations in the following words: "In camps, the contagion passes from the patient to his comrades in the same tent, and thence perhaps to the neighboring tent; the rotten straw becomes infectious; but the principal source of infection lies in privies after they have received dysenteric excrements. Hospitals also spread the disease; those who are admitted with dysentery transmit it not only to the other patients, but to the nurses and other persons waiting on them." Coste, first physician of the French army in the United States, who witnessed several epidemics of dysentery, recommended the separation of dysenterics from the other patients, in order to avoid contagion; he himself contracted the disease while examining several patients landed at Newport. Guilbert, describing the diseases which ravaged Napoleon's army in Russia and Poland, writes: "It is impossible to imagine the rapidity with which dysentery was transmitted from one patient to others occupying neighboring beds; the straw they had used was infectious; the privies were foci of these miasmata; physicians contracted the disease by examining carefully the evacuations." In 1831, dysentery developed among the Belgian troops in the camp of Diest; the patients afterwards propagated the disease in hospitals, cities, and villages where they took shelter. Gouzée relates that one of these soldiers, affected with dysentery, left the Brussels hospital to visit his family at Fekeren, where he died two days after his arrival; his eldest sister was taken ill and died eight days later; in this interval another sister fell sick and died on the ninth day. When the medical committee of the province visited the house, the last pa-

tient had just died and the autopsy showed that the trouble was dysentery. Lombard relates that in 1857 dysentery appeared in all those places in Central Russia through which the troops from the Crimea, who were infected with dysentery, passed.

Kelsch and Kiener published numerous instances of manifest contagion found in the reports of the physicians who witnessed the local epidemics in France; among others we shall call attention only to the following: In the lower Loire an epidemic of dysentery developed in 1850; in the commune of Renac, writes Dr. Blanche, there were no sick except an old man suffering from dropsy, when, on the 8th of August, there arrived a young man coming from a commune of the lower Loire to be treated for dysentery at the house of a sister; the dejections were thrown into the street; the greater part of the inhabitants of the neighboring houses were almost simultaneously taken with dysentery, and from there the disease spread throughout the commune. In Sainte Marie the contagion was more evident, because the author was able to follow it from door to door; a servant transmitted the disease to his masters, who in turn transmitted it to friends calling to see them. From Sainte Marie a young man suffering with dysentery went to visit his family in Courmont; he took the germ of the disease, which developed almost all over the commune. The reports of the physicians who witnessed the epidemics of Ebreuil, Montiervage, Villeval, Rocheless-Balmont, etc., leave no room to doubt the influence of contagion. The epidemiological history of smallpox and scarlet fever, write Kelsch and Kiener, does not furnish more evident instances of contagion.

In relation to the dysentery of warm climates, the following facts are significant enough to render unnecessary any commentary. Dr. Beauchef relates that the French ship *Loreit*, anchored on the west coast of Africa, was in the best possible sanitary conditions, not one of the crew being ill, when she was ordered to transport to Goréa the sailors of the sloop-of-war *Eagle*, among whom were twenty-nine dysenterics; a few days after, on the high sea, dysentery spread to the crew of the *Loreit*, and only ceased after all the patients had been landed at Goréa. The transport *Dryade*, also of the French navy, was commissioned to carry to Suez the patients and convalescents furnished by the hospitals of Shanghai, Hong-Kong, and Saigon; among the patients were several dysenterics. During the passage dysentery developed epidemically, spreading from man to man by proximity, and attacking even the nurses; the only persons spared were the sailors and officers who did not come near the patients. In 1893 a grave epidemic of dysentery developed on Fortuna, one of the New Hebrides group of islands in the Pacific Ocean. A labor vessel from

Queensland landed a Fortunese woman with a half-caste child suffering from dysentery. The disease soon spread and cut off one-fourth of the population. "It has destroyed so many of the children that in ten years more the Fortunese people will be extinct" (Davidson). In Brazil examples of undoubted contagion of dysentery are constantly observed in times of epidemics. In large cities it is more difficult of appreciation than in the interior, especially on farms; when dysentery develops epidemically in the country it can be followed from farm to farm, from district to district, and the appearance of the disease in a hitherto healthy locality is always seen to coincide with the arrival of a sick person, who transmits it to those with whom he is in contact. In cities the contagion can be well appreciated when dysentery develops in a collective dwelling; in Rio de Janeiro, for example, it is observed nearly every year in the lunatic asylum; in this great establishment, whose population is about eight hundred persons, the disease is propagated from individual to individual, and often attacks the nurses and physicians.

From the facts mentioned and the preceding considerations the contagious character of dysentery becomes evident, whether it be observed in the tropics or in temperate and cold countries. This character has also been officially recognized by the governments of Brazil, France, the Argentine Republic, etc., in whose sanitary regulations dysentery figures among the diseases subject to compulsory notification along with smallpox, yellow fever, cholera, etc.

But dysentery does not always present this contagious character, nor is it always transmitted with facility to persons about the patient. In the tropics this fact can be appreciated better than anywhere else; outside of the epidemic periods it is very difficult to prove the contagiousness of the disease. In Rio de Janeiro, for instance, sporadic cases of dysentery are observed all the year round; in these cases contagion is exceptional; I have frequently attended persons affected with acute or chronic dysentery who did not transmit the disease to other members of the family, to persons living in the same house, or to nurses. Contagion is not, therefore, a constant and infallible character in dysentery; this disease cannot be considered contagious in the same sense as syphilis, hydrophobia, and smallpox and other acute exanthemata. As in other infecto-contagious diseases, contagion is in dysentery a contingent property subordinate in its manifestations to the energy of the virus and other influences. Dysentery usually begins by infection, only those persons being affected who frequent contaminated places; the contagion is then much restricted and limited; at times, however, owing to special circumstances, the contagious character

becomes evident, the disease spreads from individual to individual with greater or less rapidity, and is even transmitted to a distance, creating foci here and there, spreading throughout a whole municipality, a district, a state, a country. The epidemiological study of the disease puts this fact beyond all manner of doubt; the dysentery that prevailed epidemically in France in the year 1857 invaded twenty-nine departments, causing a total of 7,119 deaths; that which developed in the middle of the present century in Sweden became generalized throughout the country, and caused more than 20,000 deaths; finally, in 1845, the disease extended throughout the central regions of Europe.

Among the causes which concur to activate the contagion of dysentery and give the disease an epidemic form, the following deserve special mention: the agglomeration of individuals, the vicissitudes of war, privations and chiefly hunger, and the greater energy of the virus producing the disease. Very often these various circumstances are united and associated. It was, for instance, by virtue of crowding and lack of food that dysentery always developed with an epidemic, contagious, and grave character on board the slave-ships in the days of negro traffic among the wretched Africans, who were crowded together and miserably fed. The influence of the agglomeration of individuals explains why dysentery is observed in tropical cities with a sporadic character, and at the same time prevails epidemically in the asylums, penitentiaries, and barracks of the same cities. Agglomeration and deprivation of food explain likewise the origin of those great and murderous epidemics which develop in hunger-stricken districts. Galen, describing the famines of the Roman empire, mentions dysentery, to which he attaches great importance. During the famine in the kingdom of Naples, in 1764, and during the famine in Algeria in 1867, it caused great ravages. In Brazil the starving emigrants from Ceará and other northern states scourged by the drought of 1879, suffered greatly from it. Finally, the agglomeration of individuals, pollution of the soil and air, errors in diet, and the greater virulence of the producing cause of the disease explain the great and grave epidemics which always prevail among armies on the march.

Bacteriology.

The infectious and contagious character of dysentery being demonstrated, and the supposition that it may originate under the influence of trifling causes being thrown aside as absurd and inadmissible according to the facts daily observed, there can be no doubt

as to the nature of the pathogenic agent of the disease. We must look for the ultimate cause of dysentery in the class of the infinitely small, of the microorganisms which enter the human system, live there, and multiply with astonishing rapidity. In this particular the great majority of modern investigators are agreed, and the parasitic nature of the disease may be considered established beyond the shadow of a doubt. The same harmony, however, does not prevail in regard to the species of the microbe, the germ which must be considered specific. A great number of microorganisms have been isolated, described, and considered as capable of producing dysentery; numerous contributions from various countries have enriched science, and from the reading of them it may be seen that dysentery is attributed now to a parasite of the nematoid class, now to infusoria, amœbæ, bacilli, diplococci, monococci, etc. This extraordinary abundance of theories is a certain indication of a want of knowledge, and proves that the pathogenic problem of dysentery cannot be considered as definitely solved. I shall recapitulate the investigation of the latest contribution on the subject, allowing greater development to the theory of amœbic parasitism, which undoubtedly has more supporters than any others. I shall not dwell on the first attempts represented by the investigations and discoveries of Prior, Ziegler, Klebs, Pfeiffer and Hallier, Condurelli, Maugeri, and Aradas; they have only an historical interest. The same may be said in relation to the Anguillula stercoralis of Normand, which has been found in different countries in the dejections of individuals affected with various diseases of the digestive tube, as well as in those of individuals in perfect health. I shall not insist on the dysenteric bacillus of Chantemesse and Widal, considered for a long time as the specific agent, since the investigations made by Baumgarten, Kartulis, and others seem to show its identity with bacterium coli.

Bacteria.—Ogata, during an epidemic which he observed in Japan in 1891, discovered in the dejections of individuals affected with dysentery a short bacillus, measuring one micromillimetre in length, the cultures of which, being administered to animals by ingestion or renal injection, provoked dysenteriform symptoms and lesions. Silvestri, in examinations which he made in Nebbiceno during an epidemic that prevailed there, found a diplococcus, the cultures of which reproduced dysentery in cats. During the grave epidemic which developed last year in Japan, Dr. Kiyoshi Shiga, assistant to Professor Kitasato, undertook rigorous investigations, and discovered a bacillus which he considers the pathogenic agent of dysentery. It is a short rod, rounded at the ends and having slow movements; morphologically considered, it is very similar to the

typhic bacillus, having, like the latter, a tendency to produce forms of involution; it is decolorized by the method of Gram, and does not form spores. On agar-agar, in twenty-four hours, large colonies are formed, which are rounded, damp, and bluish by transparency and increase constantly, assuming finally an irregular shape; on gelatin plates the colonies formed have well-defined edges, which are yellowish and finely granular; the gelatin is not liquefied. It does not coagulate milk or ferment glucose. It presents a well-defined agglutinative reaction with the serum of dysenteric patients; this reaction does not take place either with the serum of other patients or well persons or with the various curative serums. This bacillus was always found by the author in dysenteric dejections, and was also met with in the intestinal walls of two persons who had died of acute dysentery.

A great number of observers do not believe in the existence of a specific germ, and hold that the disease may be produced by the isolated or associated action of several microorganisms, some of which habitually infest the intestines, while others living outside are known to be able to determine various morbid conditions. L. Bertrand, one of the most ardent supporters of this opinion, in a recent work writes: "Dysenteric infection is polybacterial, not specific; the microbes which seem to be able to determine it, either by themselves or by their toxins, exist in the air, in water, and in the soil. Through the medium of the air, and oftener still of drinks and food, they enter the organism via both the respiratory and digestive apparatuses; they can remain there as latent and inoffensive parasites until the accidental aggravation of their virulence and certain lesions of the intestinal mucous membrane permit them to become nocive and invade the tissues." Maggiora, Courlet and Loir, Arnaud, and Celli and Fiocca admit that the bacterium coli commune can, under certain conditions of virulence, produce symptoms and lesions of dysentery. Zancarol regards the streptococcus as the etiological factor common to dysentery and abscess of the liver. According to Calmette, the streptococcus is frequently associated with the pyocyanic bacillus, and both can, either separately or together, determine the appearance of the disease.

Amœbæ.—Amœbæ, protozoa of the rhizopod class, are protoplasmic bodies formed by a hyaline enveloping membrane and a mass of granular protoplasm containing in its interior non-contractile vacuoles, varying in number from two to eight. In a state of repose amœbæ present the appearance of a sphere; they are, however, gifted with movements which are manifested by slight dislocations and by the emission of one or more pseudopodia. Their dimensions vary

from ten to fifty micromillimetres. Amœbæ live in damp ground or in waters charged with organic matter; when the medium in which they are dries, they become encysted and await more favorable conditions; when they again reach a damp medium, they leave their latent life, throw off their protecting envelope, feed, and multiply by division. Thus it is easy to conceive that they can enter the organism of man or of the lower animals, either in water or in food (Blanchard).

Lambl was the first to draw attention to the presence of amœbæ in the contents of the intestines; he observed them in 1859 in Prague in the stools of a child affected with dysentery. Lewis and Cunningham, in 1870, found numerous amœbæ in the dejections of cholera patients in Calcutta. But the nature of the parasite and the rôle it plays as an etiological factor of dysentery were not determined until 1875 by Lösch, who verified its presence in St. Petersburg in the dejections of a young peasant affected with chronic dysentery. He succeeded in provoking in a dog, by rectal injections of fecal matter loaded with amœbæ, ulcerous lesions of the large intestine, and verified, eight days after the last injection, the presence of amœbæ in the dejections of the dog.

The observations and investigations of Lösch were carefully made, and his description of the parasite, to which he gave the name of *amœba coli*, was so good that very little has been added to it since. The discovery of Lösch was verified shortly after by Leukart, Grassi, Perroncito, Sonsino, Calandruccio, and Blanchard; these authors, however, confine themselves to confirming the existence of the amœbæ as intestinal parasites, without pronouncing themselves affirmatively as to the reality of the pathogenic rôle attributed to the protozoa by Lösch. Koch, however, in the post-mortem examination of individuals who had died of dysentery in Egypt, found numerous amœbæ in the tissue at the base of the ulcers and in the matter covering the ulcers, and he concluded by admitting a relation of cause and effect between these parasites and the disease. After Lösch, Kartulis contributed most to the solution of the pathogenic problem of dysentery, considered from the point of view of amœbic parasitism. While practising in Alexandria, he had an opportunity to observe hundreds of patients, and in a series of works published in 1885, 1887, 1890, 1891, and 1893 he gives an account of his investigations and experiments. He verified in post-mortem examinations the constant presence of parasites in more than five hundred cases, not only in the fæces of dysenterics and in the pus of abscesses of the liver, but also on the surface of ulcers and in the walls of the abscesses. He never found amœbæ in other affections of the intestines,

whether ulcerous or not. He succeeded in cultivating the parasite in an infusion of sterilized dry straw, and twice provoked the disease in cats by inoculations of these cultures. The discoveries of Kartulis were confirmed by numerous observers in various countries, at least in so far as regards the presence of amœbæ in the dejections and in the intestine of dysenterics. Hlava, in sixty cases of dysentery observed in Prague, found amœbæ and produced the disease in cats and dogs by injecting fæces containing amœbæ. Massautin in Kieff, Cahen in Graz, and Nasse in Berlin, relate affirmative cases. Osler was the first to observe amœbæ in America; he found the parasites in the pus of an abscess of the liver complicated with chronic dysentery; amœbæ were also found in the fæces. After Osler's work, numerous contributions were furnished by American physicians, who observed amœbæ in the fæces and in the intestines of dysenterics; among others may be mentioned: Stengel, Musser, and Rhein of Philadelphia, Eichberg of Cincinnati, Wilson of Birmingham, Slaughter of Virginia, Stockton of Buffalo, Lewis of Baltimore. In Brazil amœbæ were observed in the fæces of dysenterics and in the pus of abscess of the liver by Lutz in S. Paulo, and by Fajardo, Chapot Prevost, and myself in Rio de Janeiro. In Europe, during the last two years, various observers have published works on amœbic parasitism in dysentery. The most valuable contributions, however, that have been made on this subject, next to those of Lösch and Kartulis, are undoubtedly the monograph of Councilman and Lafleur, and the papers of Kruse and Pasquale, and of Harris. Councilman proposed for the parasite in question the denomination of *amœba dysenteriæ*, much more significant than the name *amœba coli* given by Lösch. He writes: "The name given to it by Lösch is not distinctive; for it seems very probable that there may be a number of species of amœbæ which, under certain conditions and in certain localities, may inhabit the colon. This is evident from the work of Cunningham, who found them not only in the human fæces in health and disease, but also in the fæces of some of the domestic animals."

The *amœbæ dysenteriæ* differ somewhat in appearance according as they are active or inactive, alive or dead; when dead they resemble very much the tumefied cells of connective tissue, which often exist in great quantity in the fæces and may be mistaken for them.

The dimensions of the amœbæ vary ordinarily between fifteen and thirty-five micromillimetres; in their body may be distinguished two parts: the outer portion or ectosarc composed of a clear homogeneous substance, and the inner or endosarc composed of a highly refractive mass, and containing vacuoles of greater or less size; within the vacuoles bodies in active Brownian movements may be sometimes

seen. When in motion the appearance of the amœba is characteristic; its movements are sometimes very slow, and sometimes more or less rapid, and consist in a progressive motion or more commonly in the thrusting out and retraction of pseudopodia. Among the amœbæ are frequently found various foreign bodies; the most common of these are red blood corpuscles; then follow cells of pus, well preserved or in various stages of disorganization, bacilli, micrococci, granular detritus, etc. According to Harris, a collection of fecal detritus is often attached to the posterior portion of the amœba while it is in motion, and frequently he has been unable to make out the exact point of separation; indeed, it has seemed to him at times that there was direct continuation of one into the other. If this is true, it may explain what has always puzzled him, *i.e.*, how do the amœbæ take in their food and the various cellular elements which are almost always found in their bodies? As far as Harris' observations go, pseudopodia are never sent out at the point at which these masses are attached to the amœbæ.

More or less well-founded objections have been formulated against the amœbic etiology of dysentery. Numerous investigators, many of whom enjoy a well-merited reputation, as, for instance, Laveran, Maggiora, Ogata, Zancarol, Grassi, Celli and Fioca, Calmette, Calandruccio, Schusberg, Casagrandi and Barbagallo, Bertrand, and others combat the doctrine, not admitting the pathogenic rôle attributed to the amœbæ. They object that the parasite is often found in the fæces of healthy individuals, that it has been seen in the fæces of patients suffering from other diseases of the digestive tube, and that it is not always met with in the fæces of dysenterics. They add that the experimental attempts made at establishing the pathogenic influence of the amœbæ are subject to contestation in so far as regards the significance of the results obtained; dysentery provoked by rectal injection of dysenteric fæces is an argument of no value, for even if we admit that it has been possible to cultivate the amœbæ outside of their habitual medium no well-verified fact proves that it has been possible to separate them from their microbian associates; nothing, therefore, demonstrates that they act on the intestines without the concourse of microbes. Schuberg concludes that the abundance of amœbæ in dysentery is the effect and not the cause of the disease; the ulcerative lesions afford this habitual dweller of the intestines more favorable conditions for its development. Casagrandi and Barbagallo are still more categorical; observing that the amœbæ absorb bacteria and that in dysenteric ulcerations microbian colonies are rare at the points at which the amœbæ are observed most abundantly, they conclude that the rôle of the amœbæ in the dysenteric intestine is to combat

the microbes, in order to permit the reparation of the tissues and impede the excessive acuteness of the process. The amœba coli would thus be not a pathogenic agent, but a guardian of man's health. The partisans of amœbic parasitism reply with great advantage to all these objections. Kartulis, answering Grassi, had already maintained that the amœbæ found in fæces of healthy individuals in Italy were not precisely identical with those he had observed in Egypt. Cruse and Pasquale showed that the amœbæ of normal fæces exercise no pathogenic action whatever on cats, while the amœbæ of dysenteric dejections, morphologically similar to the former, frequently provoke diarrhœa and ulcerations when injected into the rectum of the same animal.

Quincke and Roos admit the existence of three amœbæ, parasites of the human intestine: the *amœba coli felis,* identical with the *amœba coli* of Lösch, pathogenic to cats, the animated cause of dysentery; the *amœba coli mitis,* non-pathogenic to cats, and giving to man only a simple diarrhœa without gravity, and the *amœba intestini vulgaris,* which is common and inoffensive. On the other hand, Councilman and Lafleur show that in many patients the amœbæ, not having existed in the dejections during life, are found in great abundance in the intestines at post-mortem examinations. No doubt, a great deal remains to be investigated and definitely established in relation to the biological conditions of the amœbæ; but even now everything leads us to believe either that there are various species of amœbæ, one of them being pathogenic, or that these parasites live normally as saprophytes, acquiring occasionally pathogenic qualities owing to the concourse of accessory causes.

The presence of the amœbæ in the contents of tropical abscess of the liver is, in my opinion, one of the most powerful arguments in favor of the amœbic etiology of dysentery. The physicians of the last century had already remarked the frequency of abscess of the liver in individuals suffering or having suffered from dysentery. At the beginning of this century, Annesley insisted strongly on this subject; in fifty-one autopsies of dysentery he found abscess of the liver twenty-six times. After him, the English physicians in India and the French in Algeria always verified the coincidence of the two diseases. If we take the figures furnished by the statistics of Waring, Moore, Macpherson, Marshall, Morehead, and Dutrouleau we shall have a total of 1,997 autopsies of dysentery with 407 abscesses of the liver. Dutrouleau relates that in the hospital of Saint Pierre, during a period of five years, two-thirds of the individuals who died of dysentery presented abscesses of the liver. The geographical distribution of the two diseases is identical; from this point of view

they are inseparable; in countries where dysentery is endemic and grave, suppurative hepatitis figures beside it among common diseases. When the dysenteric endemic abates, when the disease becomes sporadic and rare, abscesses of the liver are likewise rarely observed. Kelsch and Kiener collected observations on liver abscess published by practitioners of all times and places, and, throwing out the incomplete ones and availing themselves only of those that were free from all doubts, they succeeded in collecting statistics embracing 314 complete cases of suppurative hepatitis; in these there was coincidence of dysentery 268 times, which is equivalent to a proportion of more than 75 per cent. These figures are eloquent and significant enough, together with the historical and geographical coincidence of the two diseases, to authorize the assertion that they are due to the same cause and that tropical abscess of the liver has no nosographical independence, being merely an hepatic determination of the dysenteric process.

Now, in the contents of abscesses of the liver complicated with the evolution of dysentery or developing during convalescence of the latter, numerous investigators have remarked the presence of amœbæ, either in a state of isolation or associated with various bacteria. There are, however, cases of large abscess of the liver observed in patients who have not suffered from dysentery; is the affection in these cases dependent on amœbic parasitism? I do not know whether studies and investigations have been made in this sense; nevertheless, I observed in February of this year a very instructive case of the kind; it was in a woman who was under my treatment in the Misericordia Hospital; she had an immense abscess of the right lobe of the liver, and stated that she had not had diarrhœa or dysentery; more than one litre of yellowish-white pus was withdrawn from the abscess, and in this pus numerous amœbæ in active motion were seen by me and by Prof. Chapot Prevost and his assistants, Drs. Dias de Barros and Ernani Pinto. The constant presence of the amœbæ in the contents of tropical abscesses of the liver cannot but be considered a weighty argument in favor of the amœbic etiology of dysentery, provided we admit the geographical, epidemiological, and clinical coincidence of the two affections, which undoubtedly come from the same producing cause.

Some authors think that for the amœbæ to reach the liver they must have penetrated through the walls of the intestine, passed along the peritoneum, and burrowed their way through the capsule of the liver. But it seems much more probable, as Councilman and Harris affirm, that they reach the liver through the portal circulation; in support of this opinion is the fact that they are fre-

quently met with not only in the walls but also in the interior of the blood-vessels.

The principal question is to know how the amœbæ get into the human system and more precisely into the intestines, there to produce the lesions of dysentery, and go from there to the liver and determine the abscess. According to Councilman and Lafleur, they reach the large intestine in food or drink. I believe they may be taken in with the air. The food may be contaminated by the hands of persons who have been in contact with dysenterics. According to Fouquet, who made observations in Brittany, contamination by the hands is the most common mode of contagion; persons who attend to the sick frequently handle the bread, the clothes, the table, and the cooking utensils without washing their hands; hence numerous facilities for the transmission of the disease to the other members of the same family. Lardier and Prunet also insist on the propagation of the disease by means of contaminated objects.

Medical literature records numerous facts which demonstrate the important rôle of water in the dissemination of dysentery. Lalluyaux d'Ormay showed that in various localities of Cochin China it was possible to cause dysentery to appear or disappear at will, by using or discontinuing certain waters. Barthelemy, in his "Medical Report of the War of Dahomey," relates that during the first half of the campaign dysentery was not observed among the troops. The latter were then operating on the shore of the Ouemé, whose clear running water was filtered in Chamberland filters before being used. But when the army moved away from the Ouemé in the direction of Abomey, they were compelled to use swampy water without filtering; from that moment dysentery made its appearance. In Calcutta, in Secunderabad, in the Deccan, in Algeria, in the West Indies, in Carabodge, in Brazil, etc., epidemics of dysentery have always been seen to abate and disappear when the use of impure water has been discontinued. Léon Collin, who carefully studied the subject, writes: "Proofs abound and we may no longer doubt the close relation between the immunity of certain populations from dysenteric affections and the degree of purity of their water supply." The water whose use provokes dysentery does not act, as some authors think, by reason of the trifling impurities it contains; its pathogenic rôle is that of a mere vehicle of the germ producing the disease. Of great interest in this connection is certainly the case reported by Fitz and Gerry, as these observers demonstrated the presence of amœbæ in most respects resembling those found in the fæces, in a cistern the water of which the patient constantly used.

The rôle played by the air as a vehicle of the dysenteric germ can-

not be contested. As far back as the last century, Pringle recommended the avoidance of emanations of water-closets used by dysenterics. Czernicki, Pinel, Desgenettes, Coste, and others mention numerous facts proving the influence of the air in the dissemination of the disease. The following fact, recently related by Bertrand, is worthy of being recorded here: In the course of an epidemic of dysentery, two pharmacists who were not engaged in the hospital where the patients were received and treated, made the chemical analysis of dysenteric matters; the operations lasted several days and, notwithstanding they carefully cleansed their hands with antiseptics at the end of each session, they were attacked by the disease.

Meteorological Conditions.

The dysenteric germ is undoubtedly influenced by meteorological elements, and chiefly by thermal conditions. The geographical distribution of the disease evinces the influence of temperature, for although it is observed in all the inhabited regions of the globe it increases in frequency as we approach the equator, and it is in the tropics that its rule becomes constant and permanent. Even in the tropical zone it is at places where the annual thermic mean is highest that dysentery is observed with the character of a more or less persistent endemic; on the high tablelands and in the mountains the disease appears in the form of seasonal epidemics. Kelsch and Kiener assert that of all the diseases that prevail among the French population, that which is most clearly and absolutely a disease of the seasons is dysentery; the epidemics usually develop and terminate their evolution in the middle of the hot season. Out of 750 epidemics of dysentery collected by Kirsch, 529 raged in summer, 187 in autumn, 14 in winter, and 25 in spring. The regional epidemics in Europe always begin in the months of July and August, last throughout the autumn, and terminate at the beginning of winter. The estival and autumnal character of dysentery is signalized in an evident manner by military physicians. During the Seven Years' War, Monro always saw the disease commence in July, become prevalent in August and September, and then abate and disappear. Heubner, a physician in the German army during the Franco-Prussian war of 1870, gives us statistics which render conspicuous the influence of temperature on the course of dysenteric epidemics. The same fact is signalized in the medical reports on the wars of Italy and the Crimea; but the most important document to be consulted on the character of dysentery as a disease of the seasons in armies on the march, is undoubtedly the official statistics of the Federal army in the war of the rebellion in America.

The influence of the seasons is less conspicuous in warm climates, especially in places where the annual thermal mean is above 23° C. (73.4° F.); there the endemic remains permanent during the whole year, with slight recrudescences in summer; that is what is observed, for instance, in Senegal, in Cochin China, in the North of Brazil, in Martinique, in Cayenne, etc. According to Dutrouleau of 100 deaths from dysentery in Martinique, 18.76 took place from January to March, 20.55 from April to June, 27.73 from July to September, and 32.96 from October to December.

Atmospheric vicissitudes and exposure to cold and wet were formerly considered by various observers as causes capable of provoking dysentery. This opinion is now completely abandoned. Sudden exposure to cold when one is overheated, exposure to the night air, the wearing of wet clothes, sleeping on the damp ground, etc., can indeed provoke a derangement of the digestion, a non-specific diarrhœic flux, putting the system in a bad condition to resist the producing agent, and acting, therefore, as predisposing causes. Rains, winds, the hygrometric state of the air, storms, and the presence of a greater or a less amount of ozone in the atmosphere do not seem to exercise any influence on the genesis of dysenteric epidemics and on the endemic recrudescence.

Personal Conditions.

Age.—Dysentery is observed at all ages; the tables of statistics always contain a greater number of adults, because these are more exposed to the causes of the disease. It is, on the other hand, more grave in children; according to Davidson, in 1878 the dysenteric death rate of the army at India was 1.73 per 1,000, that of the European children was 3.84 per 1,000. In Brazil, especially in Rio de Janeiro, simple diarrhœas are very frequent in children; dysentery, on the contrary, is rare.

Sex.—Both sexes are equally predisposed to contract dysentery. Waring thinks that women are more predisposed than men; other authors assert the contrary. Statistical tables generally contain a smaller number of women; this is undoubtedly due to the fact that they are less exposed than men to the determining cause of the disease.

Races.—No race enjoys immunity from dysentery; they all pay their tribute to it. The liability of the races to contract the disease seems to vary according to the countries in which it is observed. In Calcutta, according to Corre, in 1,000 individuals of the civil population the morbidity is estimated at 0.05 among the Europeans, 0.10 among the mixed races, and 2.02 among the Hindoos. In Madras,

in 1,000 men of the effective service, the fatality oscillates between 8.90 and 70.30 among the white troops, and between 4.20 and 12.10 among the native troops. In the United States, according to Harris, race seems to be an important etiological factor; in 68 cases collected by him only 18 occurred in the colored race. In Brazil, dysentery is observed in all the races that constitute the population of the country; perhaps indeed the black race is the most predisposed, not on account of any racial distinction, but because the negroes are the most exposed to other predisposing causes of the disease, such as defective diet, want of cleanliness and hygiene, etc.

Acclimation.

A long sojourn in endemic centres will not confer immunity from dysentery; on the contrary, according to some observers, the longer the time of residence of a European in the colonies, the more predisposed he is to contract the disease. In Martinique, writes Rufz, more dysenterics are found among the soldiers of the garrison who have remained on the island several years than among the sailors who go and come, staying only a short time; the cases are also less grave among the latter. In India, writes Davidson, the troops, during the first two or three years of their sojourn, show a somewhat greater liability to the disease than those who have been longer in the country; but after the seventh year the deaths from dysentery begin to increase, and they go on increasing according to the length of service. This will be seen by the following figures, from a table prepared by Bryden, showing the ratio of deaths from dysentery to one hundred deaths from all causes among soldiers, according to length of service:

First year	9.6	per cent.
Second year	10.4	"
First five years	9	"
Fifth to seventh year	10.1	"
Above seven years	13.3	"
Above ten years	13.7	"

This table proves that there is no acclimation for dysentery.

A first attack of the disease does not confer immunity against new attacks; on the contrary, it is very common to see individuals who have had five, six, or more dysenteric attacks.

Errors in Diet.—Persons who suffer from a want of food, or who live on food of bad quality, are the most subject to contract the disease. "Dysentery," writes Harris, "is a disease preëminently of the poor and is almost always associated with filth, bad hygienic surroundings, and lack of proper food." It is constantly observed in famine-

stricken communities, and was formerly very frequent among the slaves in Brazil. According to Gestin, one of the causes that contributed most to the dissemination of the epidemic in Pont-Aven (France), in 1856, was the very defective alimentary hygiene. According to Fouquet, in Brittany, during the most violent epidemics, dysentery does not enter the castles and the houses of the wealthy burgesses, even those situated in the heart of the invaded territory; and if it does happen to get in, it attacks only the servants and dependents, sparing the masters and their children. I have observed dysentery in Brazil in persons of the best society, who live on the best food and are surrounded with every comfort; nevertheless, I recognize that in this country it is most frequent among the poor, and chiefly among people who live under bad hygienic conditions, or who live on poor diet and drink impure water.

A lack of food and the use of deteriorated or improper food irritate the intestinal mucous membrane, provoking catarrh; thus the way is opened to dysenteric infection. In like manner the attacks of diarrhœa and enteritis which often precede the appearance of dysentery act as predisposing causes.

Pathological Anatomy.

The specificity of dysentery, demonstrated by the study of the causes that preside over its genesis, is absolutely confirmed by post-mortem examination. Thanks to investigations effected in the first half of the present century by the physicians who observed the regional epidemics in France, and by those who practised in the endemial zones of the disease; thanks to the excellent descriptions of Heubner, Cornil, Kelsch and Kiener, and to the recent contributions of Councilman and Lafleur, and Harris, the pathological anatomy of dysentery is perfectly well understood. It is true that in relation to certain details of the anatomical process the descriptions do not completely agree; the opinions emitted are sometimes widely different, not to say contradictory; but in all the descriptions we find the specific and characteristic lesion of dysentery—the ulcer *en bouton de chemise* of Kelsch and Kiener, the undermined ulcer of Councilman and Lafleur. The divergences observed in the post-mortem examinations performed by various investigators need not cause surprise if we bear in mind the more or less important rôle that microorganisms foreign to the disease, normally inhabiting the intestine or reaching it accidentally, play in the anatomical process of dysentery. Now the concourse of these last factors is not always the same at all places and in all individuals; whence certain differences signalized in relation to

the extension and character of the lesion and other details of the process.

The post-mortem examination furnishes somewhat different results, according as the dysentery has had an acute or a chronic evolution; it is, therefore, highly proper to study separately the lesions of acute and those of chronic dysentery.

Acute Dysentery.

Kelsch and Kiener group the lesions under two typical anatomical forms, the ulcerous and the gangrenous, which, according to them, correspond to two distinct modalities of the necrosis of the tissues—dry necrosis and gangrene. Gangrene of the intestines is considered by nearly all modern authors as an anatomical character of dysentery, chiefly of tropical dysentery. It is signalized in the descriptions of Annesley and other physicians of the first half of the present century, but it was chiefly Dutrouleau and Kelsch and Kiener who insisted most on the subject. Davidson in a recent work writes: "Grangrene of the mucous, or of the mucous and submucous, coats is one of the commonest and most characteristic lesions in chronic dysentery." Nevertheless, in many localities in the tropics, gangrene of the intestine has not been observed, or is seen exceptionally. Hunter stated that he had never seen gangrene or abrasions of the villous coat in Jamaica. Dutrouleau himself, who considers gangrene a characteristic lesion of tropical dysentery, met with it only in the Antilles and in Senegal; in Guiana, adds he, the disease is much milder. In Brazil, and chiefly in Rio de Janeiro, gangrene is very rare; I have never had occasion to observe it, though numerous cases of acute dysentery come under my attention every year. If we pass from the tropics to the temperate regions we shall see that the dysentery which develops in small seasonal epidemics is exceptionally accompanied by gangrene; the same, however, is not true in regard to the epidemic dysentery of armies on the march, where the crowding and the surrounding conditions pollute the soil and air. Since then gangrene of the intestine is rare and exceptional in many localities where dysentery prevails endemically, and since in others it is observed only under certain and determined conditions, it does not appear to me logical and rational to regard it as of a nosographical character, as a specific lesion of the disease. Gangrene is certainly not a lesion determined by the amœba dysenteriæ, but is rather owing to the action of bacteria foreign to the dysenteric process, and it must therefore be regarded as a complication of the dysentery and not as a specific lesion. I shall describe only one anatomical form of acute

dysentery, the ulcerous form, which, according to the case, is more or less extensive and intense, and is sometimes complicated with gangrene.

The peritoneum may be perfectly normal, but in most cases it is highly injected or cloudy. Inflammation of the peritoneum is frequent when the disease is complicated with gangrene; the peritonitis is almost always consecutive to a perforation. It may be partial or general; in the first case, if there is a perforation, a collection of pus will be found at that point, circumscribed by adhesions to the intestinal folds which are themselves agglutinated together; in the second case, which is the most frequent, pus is found in the peritoneal cavity, sometimes in considerable quantity, or there is a dark liquid with a strong fecal odor. The intestine is generally found to be contracted and of a rosy color. When there is gangrene, the large intestine is voluminous and distended by gases; on its external surface are sometimes found circumscribed patches of a dark red or brown color and perforated in the centre; these patches correspond to eschars involving the entire thickness of the wall; at some points these walls are thickened, but at others they are so thin and friable as to be easily broken during removal.

The intestinal cavity contains ordinarily semisolid fecal matter, or liquid matter holding mucus in abundance, blood, and bile. The lesions are usually found throughout the entire large intestine from the rectum to the cæcum, but do not go beyond the ileocæcal valve; in some cases, however, the small intestine is involved, the lesions extending to the last portion of the ileum. The starting-point of the dysenteric process may be the cæcum or the rectum; commonly the lesions have a descending course and become graver and deeper as they approach the rectum. Bérenger-Féraud says that in the Antilles the disease generally commences in the cæcum and ascending colon, while in Cochin China it is more common to see it begin in the rectum or sigmoid flexure.

The large intestine is always found to be thickened; this thickening, which is more or less pronounced according to the cases, sometimes involves all the coats, predominating, however, in the submucosa; at other times it remains confined to the submucous coat. The surface of the mucosa, when washed, presents a bright red color at some points and a dark red color at others; it shows elevations and depressions corresponding to the folds of the mucosa, which are more voluminous and thick than in the normal condition. Over the mucous membrane are disseminated small red nodules of various sizes, from the size of a grain of flax to that of a pea; besides these small elevations are found more or less numerous ulcers of various forms

and dimensions, some being superficial and others deep, extending almost continuously from the rectum to the ileocæcal valve, or remaining confined to limited areas.

The nodosities which are found on the mucosa and which seem to constitute a starting-point for the ulcers were observed by John Hunter in autopsies performed on cadavers of persons dead of dysentery in Jamaica. "There is first formed," writes he, "a small round tubercle of a reddish color, and not larger than one-tenth of an inch in diameter. In this stage there appears a small crack on the top, with a small depression, which gradually enlarges. On examining the contents of the little tumor, I have found it a cheese-like substance. The pustule is seated under the villous coat, between that and the muscular coat. As the opening enlarges the edges become prominent and the base rough and scabious. From the base matter oozes which is sometimes tinged with blood. Such is the progress of one; but they are often in clusters, and become confluent, so as to form a rough, unequal, ulcerated surface with a hard and thickened base. Sometimes they appear like a small eating ulcer, in which the prominence of the edges gives an appearance of a loss of substance, as if the villous coats were entirely removed."

According to Kelsch and Kiener, the small nodules, when new, have a uniform red color and a somewhat soft consistence; when old, they have a firmer and more friable consistence. Their apex is transformed into a small, dry, yellow eschar, which in a more advanced stage embraces all the central part, and falls out in a manner similar to the core of a furuncle. In some cases the papulous form is not so clearly defined; the lesion presents itself as a yellow, friable, and dry eschar, which, at first small and superficial, gradually increases in size and depth. Kelsch and Kiener are of opinion that these nodosities, which they call *dry eschars,* represent the initial lesion of dysentery. Histologically there may be distinguished in them three zones: the central zone corresponds to the yellow and friable portion, in which no distinct anatomical element is to be met with and only a granular matter which is refractory to coloring-agents. In the middle zone are seen the elements of the tissue still retaining its form, but dead; the epithelia of the mucosa are transformed, deprived of nuclei, and stain highly with carmine; the fixed cells of the connective tissue are pale, without nuclei, and often reduced to granular detritus; in certain cases the tissue is infiltrated with leucocytes and has the characters of necrosis; in other cases the sanguineous extravasations fill all the interstices of the tissue. In the external zone, which is more or less extensive and more or less diffuse, according to the case, may be recognized the

characters of œdema with fibrinous coagulation of the lymph in the interstices of the connective tissue; this tissue is still alive; a few thrombosed vessels having vitreous walls, however, are found in it scattered here and there, and some dead cells. This œdema is sometimes attended with hyperæmia, diapedesis, and hemorrhages.

According to Councilman and Lafleur, the surface of the mucosa presents sharply circumscribed, projecting nodular thickenings of various size, in which are observed cavities filled with a gelatinous pus, communicating with the surface of the mucous membrane by small openings, frequently no larger than the head of a pin, but sometimes much larger. There are also sinuous tracts, sometimes representing an extension of the cavity, sometimes communicating with neighboring cavities, all filled with the same glairy gelatinous material.

The ulcers are seated chiefly on the folds of the mucosa; they are commonly oblong and lie transversely to the great axis of the colon; they may be also circular, sinuous, or irregular. They vary much in size, some not being larger than a pin's head, while others sometimes assume a diameter of two inches. Intermediary sizes are more frequent. Not infrequently a great many small ulcers are seen together and meeting at one point, which gives to the tissues the aspect of a skimmer or honeycomb. As regards the depth, the ulcers usually extend through the submucous coat; sometimes, however, they only involve the mucosa; exceptionally the floor of the ulcer is found to be formed of the thickened peritoneum. In the larger ulcers the muscular coats are frequently dissected up for some distance. When the ulcer embraces only the mucosa, which is not very common, the submucous coat is always affected; it presents itself swollen and œdematous, not only at the base of the ulcer, but at neighboring points which do not correspond to ulcerations of the mucosa.

Ordinarily the ulcer, after having perforated the mucous coat to an inconsiderable extent, reaches the submucosa and then spreads along the surface a certain distance, undermining the mucosa above, which is relatively healthy. The appearance of these ulcers is very characteristic. More or less considerable sloughing of the mucosa may take place, and also fistulous tracts are formed, which cause several neighboring ulcers to communicate. Growing in the submucosa by gradual softening and disintegration of the tissue, a veritable molecular destruction, the ulcer generally finds a barrier opposed by the muscular coat. Nevertheless, the upper layers can, in certain cases, become necrotic; the cellular infiltration then spreads to them, and the process of destruction advances and involves all the muscular coat; masses of muscular tissue slough off and are found in the stools.

According to Harris, at the centre of the ulcers the muscularis mucosæ is always broken down, but it suffers much less than the tissue beneath, and may be often seen to extend in a comparatively healthy condition beyond the mucosa, thus covering the broken-down tissue beneath. That part of the muscularis mucosæ which hangs over the ulcer is swollen, and towards the free end the fibres are granular and their nuclei are for the most part gone or entirely absent.

On the surface of the ulcers there is always found a gelatinous material which can be wiped away, leaving the ulcer clean. When examined fresh under the microscope it is found to contain amœbæ, large round swollen cells, red corpuscles, and pus cells. These cells are also found scattered through the thickened tissue of the submucosa, being more numerous at the points where the morbid process is more advanced; they seem to be connective-tissue cells which have become free by softening of the tissue around them.

Sometimes the base and sides of the ulcers, as well as the fistulous tracts, are covered by a homogeneous refracting material, disposed in bands in the form of a reticule, with oval meshes, of about the same size and containing leucocytes and lymphoid cells. According to Kelsch and Kiener, they are leuocytes which accumulate in more or less dense agglomerations, and then, undergoing a vitreous transformation, conglomerate to form reticulated pseudomembranes, adhering to the wall and similar to diphtheritic pseudomembranes. According to Councilman and Lafleur, the reticulum seems to be rather a form of degeneration of the connective tissue; in sections stained with Weigert's fibrin stain it remains uncolored; it forms a smooth covering to the edge of the ulcer, and extends in places some little distance into the tissue beneath; it especially involves the walls of vessels in its vicinity.

The blood-vessels always present more or less marked lesions; they are frequently thrombosed. The walls of the arteries are thickened and infiltrated with round cells, and there is an active proliferation of the cells of the endothelium; in the arteries are often found the alterations of obliterating endarteritis in a more or less marked degree. The walls of the veins are likewise infiltrated with round cells and undergo regressive degenerations, which facilitate their rupture. According to Harris an amœba may occasionally be seen in the act of penetrating the walls of the veins, part of the body being within and part without the lumen of the vessel. The lymphatics are always dilated.

The lesions of the mucosa, at a certain distance from the ulcers, are in general little accentuated. Very intense hyperæmia of the tissue is noticed, particularly in the superficial layer, hypersecre-

tion of mucus, accumulation of leucocytes, and frequently interstitial hemorrhages. The layer of epithelium on the surface is commonly wanting; the glands are dilated and their calyciform cells are full of mucus. At the edges of the ulcers the blood-vessels are dilated and contain numerous leucocytes. According to Councilman and Lafleur, in the cases characterized by the formation of cavities in the submucous tissue, the roof of the cavity is often entirely covered by a new formation of epithelium which had grown downwards from the mucous membrane. In most of the ulcers there was not only this proliferation of the epithelium, but the entire mucous surface was folded and turned in over the ulcer. The amœbæ are frequently found in the lower part of the mucous membrane, between and sometimes in the glands. The solitary follicles, at a distance from the ulcers, are more or less normal; in the neighborhood of the ulcers they are swollen, hyperæmic, and a little softer than in the normal state. The rôle they play in the phlegmasic and ulcerous process seems to be passive.

According to Councilman and Lafleur, it is possible to divide the ulcers into four forms: First, ulcers characterized by purulent infiltration, softening, and cavity formation in the mucosa; these have a small opening on the mucous membrane, and often communicate with neighboring ulcers by passages in the submucosa; Second, ulcers with slight undermining of the edges representing simply excavations in the thickened submucous tissue; Third, ulcers with smooth sides and clean bases; Fourth, ulcers with extensive sloughs adhering to the sides. Harris describes two anatomical forms of ulcers found in dysentery. In the first, which is the most frequent and may be considered the typical intestinal lesion of the disease, changes in the submucosa may be traced in advance of the surface ulceration for quite a distance, thus undermining the comparatively healthy mucosa above. In the second, the ulcers increase in size by gradual softening and breaking down at the surface, never by necrosis and sloughing of the underlying tissues. They sometimes do not extend deeper than half through the mucosa, but generally reach into the submucosa; they rarely extend to the circular muscular layer, and never deeper. These ulcers never contain amœbæ.

It is difficult to say precisely what is the starting-point of the ulcers and how they begin. According to Kelsch and Kiener, the initial lesion of ulcerous dysentery is the dry eschar, that is, the necrosis of a circumscribed portion of the intestinal wall, involving sometimes at once the mucosa and part of the submucosa, but oftener progressing slowly from the surface downwards. They compare it to that dry necrosis in which the form of the elements is momentarily

maintained, to which Cohnheim gave the name of necrosis of coagulation. The eschar either separates from the underlying tissue all at once, or comes off little by little, and thus the ulcer is formed.

According to Councilman and Lafleur, the process is essentially one of advancing infiltration and softening in the submucous and intermuscular tissue, with subsequent necrosis of the overlying tissue. The amœbæ reach the submucosa, producing but few lesions in the mucous membrane, and the essential changes are produced in the submucosa, the mucous membrane being attacked from below. So far as could be seen, the changes which they produce in the mucous membrane are an œdema with some fibrin formation and occasionally necrosis. The œdematous tissue then softens, the mucous membrane is broken through, and the ulcer forms.

When dysentery is complicated with gangrene, besides the ulcer described, there are others with a gangrenous character. The gangrene is not limited to the ulcers; on the brown or reddish œdematious mucosa are found gangrenous patches, more or less rounded, of a dark color, soft, moist, of a characteristic odor, and of various sizes, sometimes being as large as the palm of the hand or even larger, and occupying a large segment of the intestine. On incising these patches the gangrene is seen to have invaded also a part of the submucosa, the latter being infiltrated with pus, a purulent sanies running from it. The mucosa is detached over a considerable area; during life entire segments of the intestinal mucosa are detached and eliminated by the dejections. Haspel, who gave a good description of the submucous phlegmon, writes: "When the suppuration of the submucous connective tissue has invaded a large extent of the intestine, the mucosa is detached in large pieces, sometimes from the whole circumference of the gut, in the form of tubes, formerly mistaken for false membranes."

When the gangrenous eschar is detached and falls off, it leaves a suppurating ulcer with a soft and ragged bottom, which continues to spread. Sometimes it extends superficially, and spreads along the submucosa to a certain distance, the lesion of the mucosa remaining stationary; more or less extensive separations of the mucosa are thus produced; sometimes it extends in depth, invading the muscular and the serous coats, and determines perforations of the intestines, attended with acute peritonitis. The gangrene may also develop in a preëxisting ulcer and then it increases in surface and depth the losses of substance occasioned by the former process. In Kelsch and Kiener's book there is an illustration representing this association; in the centre of a gangrenous ulcer is a dry and cohering eschar attached to the base of the ulcer by a slender pedicle.

Chronic Dysentery.

On opening the abdominal cavity, the peritoneum is found thickened and presenting a diffuse slaty pigmentation; areas of adhesive peritonitis attach the large intestine to the wall of the abdomen or to the neighboring organs, with or without displacements. Annesley insisted much on these deformations and displacements produced by the adherence of the intestine to itself and to the neighboring viscera. Cicatricial narrowings are not infrequently observed along the tract of the intestine, almost always attended with dilatation of the portion situated above. The intestine is ordinarily pale with slate-colored spots; its walls are thick, hard, and resistant to the touch. The intestinal surface presents a pale rosy or slate color. When death results from an acute attack, more or less intense hyperæmia is observed, as well as other lesions, already signalized.

Ordinarily in chronic dysentery the ulcers met with are in different and even extreme stages of their anatomical evolution; along with furunculous nodosities and small ulcers in a stage of formation are found old ulcers with flat bottom and callous edges; along with excavated ulcers in a progressive stage are found cicatrices. In most cases the ulcers are discrete and assembled in groups separated by more or less extensive healthy segments of the intestine; sometimes, however, in certain portions of the intestine the ulcers become confluent and are attended with diffuse lesions which occasion grave disorders. The old ulcers may be round, elliptical, transverse, or serpiginous; they have thickened and callous edges. Sometimes they are superficial, showing a greater tendency to spread on the surface than in depth; they involve the mucosa and part of the submucosa; they rarely extend to the circular muscular layer. In the neighborhood there are no hyperæmia and no œdema; there is, however, an increase of fibrous tissue. Others present themselves with the characters of the undermined ulcers already described, having stopped in their evolution and begun to undergo a process of reparation. The lesions predominate then in the submucosa and may involve the muscular layer. The increase of fibrous tissue in the neighborhood of the ulcers indicates in these cases the chronic nature of the process.

The mucous glands are found dilated and full of mucus; the epithelial cells in them are full of mucus. In some places are seen glandular cysts of considerable size, probably formed by the confluence of neighboring glands. In other places the glands almost disappear, only traces of them being found; the mucosa is found to be thickened

and filled with round cells. The submucosa is always found thickened; in some places it is œdematous and in almost the whole of its extent it is transformed into dense fibrous tissue which predominates chiefly at the situation of the cicatrices, of the narrowings, and of the ulcers in which the process of reparation has begun.

Cicatrization of the Ulcers.

In acute dysentery the ulcers do not always present an invading and destroying tendency; frequently, after a progressive evolution of variable duration, the necrosis becomes limited and the ulcer undergoes a process of repair, which may terminate by the formation of a cicatrix. In chronic dysentery this process is more easily appreciated, because in post-mortem examinations, along with the ulcers in activity, some are found undergoing cicatrization and others already cicatrized. It is easy to understand that the peristaltic movements of the intestines and the irritation caused by the passage of the fæces must render difficult and retard the cicatrization. The repair seems to be effected by the formation on the surface of the ulcers of a layer of embryonic tissue more or less rich in vessels. According to Kelsch, the embryonic tissue is sometimes wanting, and the base of the cicatrized ulcer is constituted by a fibrous tissue. If the loss of substance has been small the cicatrix is represented by a bluish or pigmented spot; the cicatricial retraction brings the neighboring mucous membrane over the ulcer. If the loss of substance was large, the healthy mucosa over the ulcerated submucosa becomes depressed and engrafted over the base of the ulcer; the place occupied by the part of the mucosa destroyed by the ulcerative process is supplied by embryonic tissue with a tendency to fibrous organization.

Lesions of Other Organs.

Liver.—The liver is often found altered; its lesions, however, vary a great deal in different individuals, and it may be said that they vary likewise with the localities and the epidemic epochs. Annesley and nearly all the French authors who have treated of tropical dysentery mention hyperæmia and tumefaction of the liver as a constant lesion in the acute forms of the disease. During the life of the patient the increase of the volume of the liver is not often observed; and in many cases which terminate by recovery the patients do not mention any symptom denoting an hepatic alteration, whence it may be concluded that the liver suffered no lesions, or if any, that they were so small as not to trouble sensibly the action of the organ, and

were quickly repaired. In post-mortem examinations the liver is sometimes found perfectly normal. In chronic dysentery it is generally found diminished in volume and atrophied, weighing from 1,000 to 1,400 gm. In the acute forms of the disease it is found of a normal size or a little broader; sometimes congested and of a dark red color, at other times pale and in some cases of a dark yellow color. When dysentery is complicated with gangrene, the liver is almost always found greatly increased in volume, tumefied, soft and friable, and of a dark color with yellowish spots, some of which are raised above the surface. Histological examination reveals the presence of a superabundance of fat in the hepatic cells, and a great many small round abscesses are found disposed around the capillaries. These abscesses are of pyæmic origin, very probably resulting from microbic embolism. Together with these abscesses may be found others, differing widely from them by their seat and size and the nature of their contents; they are the dysenteric abscesses of the liver, most frequently met with in acute dysentery without gangrenous complication and in chronic dysentery.

The dysenteric abscesses may be small, of medium size, or large. They vary extraordinarily in size; the small ones are less than a centimetre in diameter and may even be almost microscopical; they are

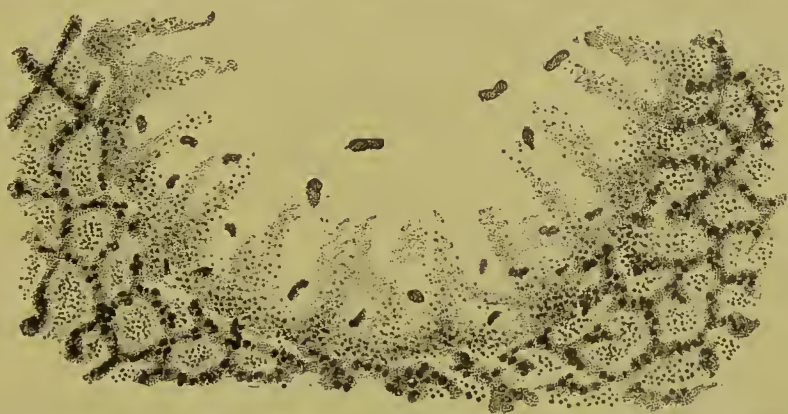

FIG. 10.—Abscess of the Liver. The liver tissue is necrotic and invaded by amœbæ and leucocytes. In the neighboring lobules the capillaries are seen to be greatly dilated. × 150.

seated chiefly in the right lobe of the liver near the surface; in some cases they are a little deeper. Sometimes they are separated from the capsule by a narrow portion of hepatic tissue; in most cases they are found immediately below the capsule which at these points is slightly thickened. The contents of these abscesses is a translucent, viscous liquid, containing a few pus cells or leucocytes, a few red blood corpuscles, broken hepatic cells, a great quantity of granular fatty matter, and numerous amœbæ in active motion. According to Councilman and Lafleur, it cannot be said that there is a definite

wall in these abscesses. The liver tissue passes gradually into the abscess, and the contour of the edge is most irregular, sometimes extending into the liver tissue for a distance of several lobules. In all cases wherever the abscess encroaches upon the intralobular tissue, this gives way before the destructive process, and the abscess extends further. The portal tissue offers much more resistance and the abscess extends around it. Around the small abscesses the hepatic tissue is usually paler than when in a normal condition. In the neighborhood of these abscesses and sometimes all through the liver is found an extensive necrosis of the hepatic cells. Councilman and Lafleur minutely described this alteration to which they attach great importance. According to them, the necrotic cells in the neighborhood of the abscesses rapidly lose their shape, soften, and become a part of the general abscess contents. The softening extends into the parenchyma and around the unaltered portal tissue, which is in this way separated from the surrounding tissue, and forms a solid mass in the abscess.

The middle-sized abscesses are found beside the small ones; sometimes the liver contains only one; ordinarily there are more, from five to fourteen being found scattered about; they commonly measure from one to five centimetres in diameter; their favorite seat is likewise the right lobe, and they are oftener superficial than deep. Their contents are identical with those of the small abscesses, perhaps a little less translucent; their walls are fibrous. In their neighborhood the hepatic tissue is nearly always congested and firmer than normally; sometimes new formation of connective tissue is observed, as well as dilatation of the blood-vessels and bile ducts, and sometimes a new formation of ducts.

The large abscess, also called tropical abscess of the liver, is mostly observed in chronic dysentery. When the disease has an acute evolution and terminates by recovery, the large abscess may be observed during convalescence; when acute dysentery terminates in death, it is exceptional to find a large abscess. In most cases it is solitary and may be accompanied by small abscesses in the neighborhood; in some cases, however, two, three, or four voluminous abscesses are found scattered about the gland. Its favorite seat is the right lobe of the liver; in eighty per cent. of the cases it is localized there, in sixteen per cent. it is found in the epigastric lobe, and in four per cent. in the middle lobe. Its size varies a great deal; there are cases in which the whole of the right lobe of the liver is found almost entirely destroyed, the capsule constituting in many points the only wall of the abscess. Ordinarily a large abscess contains between 400 and 600 grams of pus, but this quantity varies

with the size of the abscess; it may be smaller, larger, or even much larger. Annesley relates, for example, various cases of abscesses that contained as much as three litres, or six pints, of pus. Dr. Alexandre del Rio says that in Chili it is not exceptional to obtain at the first puncture or opening of the abscess from five to eight litres (quarts) of pus. Lavigerie and Haspel found foci containing eight litres, and Toman, quoted by Labadie-Lagrave, observed in Liverpool an abscess from which were extracted eighteen litres of pus.

The contents of these abscesses cannot be exactly described as pus, although very similar to it. We find a liquid, sometimes creamy and homogeneous, sometimes serous and sticky, of a reddish-yellow color in some cases, presenting in others a dark red chocolate color, and in others being white and greenish. Microscopical examination reveals the presence of a few pus cells, a great quantity of fatty granules and necrotic and destroyed hepatic cells, a few red blood corpuscles, a great many amœbæ, and sometimes cocci and bacilli.

FIG. 11.—Amœbæ from an Abscess of the Liver. ×750.

The abscess once established, it grows in two ways; first, by the softening and liquefaction of the surrounding tissue, which is already for the greater part necrotic; second, by the formation of small, separate abscesses in the neighborhood, which soon become a part of the large one. This last possesses well-defined though very irregular walls; these are anfractuous, giving insertion to villosities and ramified fibrovascular filaments; sometimes they have a ragged appearance. The internal face is covered with a smooth soft membrane of embryonic structure.

Figs. 10 and 11, for which I am indebted to my learned colleague A. Lutz, refer to a case of abscess of the liver observed by him in S. Paulo. In Fig. 10 the tissue of the liver is seen necrotic and invaded by leucocytes and amœbæ; the capillaries are much dilated. In Fig. 11 the amœbæ are seen under a higher power.

The tropical abscess of the liver may issue externally, or it may burst into the lungs or stomach or any part of the intestinal canal, or even into the adjacent serous cavities; but it shows a much greater

tendency to burst into the lung than into the bowel or peritoneal cavity.

Lungs.—In acute dysentery, and chiefly in dysentery with gangrene, the lungs are found altered. These lesions, however—congestion of the dependent parts, hypostatic pneumonia, etc.—are in no way specific. When an hepatic abscess bursts into the lung, more or less pronounced lesions are found there, affecting the pleura, the bronchia, and even the pulmonary alveolus. According to Councilman and Lafleur, abscesses secondary to abscesses of the upper surface of the liver are sometimes found in the lung.

Kidneys and Spleen.—The kidneys and the spleen are commonly found normal in acute dysentery, but diminished in volume and somewhat atrophied in chronic dysentery. In some acute cases the kidneys may be found altered. Kelsch found them increased in volume, congested, and presenting the character of diffuse nephritis. Generally, however, the changes are limited to a dilatation of the vessels and a cloudy swelling of the tubules with slight fatty degeneration.

Cellular Tissue and Muscles.—The external habitus reveals emaciation, which may be extremely pronounced when the dysentery has had a somewhat long duration. The tissues are found bloodless and dry, the subcutaneous adipose tissue disappears, and the muscles are atrophied. In chronic dysentery there is sometimes œdema of the lower members.

Symptoms.

Having for its anatomical substratum an ulcerous inflammation of the large intestine, dysentery must be clinically expressed by symptoms indicating the suffering of the affected part and of the other organs having close anatomical connections or functional solidarity with it. Indeed the principal and most characteristic symptoms of the disease are furnished by the digestive apparatus and chiefly by the examination of the intestines and fæces. These symptoms, however, vary in a very sensible degree according as the disease follows an acute or a chronic course, hence the convenience of describing acute dysentery and chronic dysentery separately

Acute Dysentery.

Acute dysentery may begin suddenly, without premonitory symptoms. The patient, in the enjoyment of apparently good health, is suddenly taken with abdominal colic and diarrhœa attended or not with cold chills, vague pains through the body, and fever; the stools

are at first abundant, frequent, and watery; shortly after, they become less abundant, mucous, and contain blood. In the great majority of cases, however, the attack is preceded by *premonitory symptoms*, which vary greatly from one patient to another; sometimes the patient complains during several days of loss of appetite, a general feeling of uneasiness and fatigue, alternation of constipation and diarrhœa, etc.; sometimes the commencement is marked by febrile or apyretic gastric derangement, with nausea and vomiting; sometimes it is a real indigestion, provoked by a cold or by indigestible food, usually coming on in the middle of the night; and sometimes it is a simple or bilious indolent apyretic diarrhœa, the first cause of which the patient cannot determine.

The Stools.—Whether preceded by premonitory symptoms or not, dysentery is usually expressed at the beginning by a more or less violent irritation of the mucosa of the large intestine; the hypersecretion of Lieberkühn's glands is shown by the mucous dejecta. The mucus is excreted in the form of vitreous, semitransparent, gelatinous, colorless or whitish masses, sometimes tinged with blood, and sometimes having a greenish color by being mixed with the bile, and always rich in leucocytes and red blood corpuscles.

When the disease is once established, the evacuations increase in frequency, the patient goes to stool from twenty to seventy times during the twenty-four hours, and sometimes even oftener. The calls to stool become more and more frequent, and are preceded by rumbling and colicky pains accompanied by straining or tenesmus. The motions which at first were abundant are now scanty; after painful efforts, the patient is able to expel a small quantity, about a teaspoonful, of pure mucus or of mucus mixed with blood, and in some rare cases a few hard masses of fecal matter or scybala. The dejecta do not always exhibit these characters; as the disease develops, they change their appearance and vary considerably in frequency, quantity, consistence, and character, not only according to the greater or less severity of the intestinal lesions, but also from day to day in individual cases; not infrequently great differences are observed in the dejecta of the same day. Intermissions and exacerbations of the diarrhœa are sometimes observed in the course of the dysentery. During one, two, or three days the patient has no evacuation and he feels well, supposing himself cured, or complains only of slight pains along the region of the colon; then the diarrhœa returns, preceded by violent colics and accompanied by tenesmus. At other times, during several days, the stools seem to be in a way to regain their normal appearance and consistence; the patient has only one or two motions a day, and without colic; the fæces are soft or even

formed. The periods of exacerbation may begin gradually or abruptly, and may last for two days, a week, or even longer, according to the case. The variety in the appearance of the dejections and their irregularities constitute characteristic features of dysentery.

The stools may be simply mucous, that is, composed of transparent or whitish mucus; this appearance is observed chiefly at the outset of the disease; the mucus is found diffluent or as viscous masses or grumous flakes, and sometimes exhibiting the appearance of rolled-up membranes. The mucus is almost always mixed with blood, and the stools are muco-sanguineous; after great efforts the patient evacuates a small quantity of matter, resembling in volume and appearance a bit of phlegm, and composed of viscous mucus with streaks of blood, or of a rosy tint. In some cases the dejections are hemorrhagic, that is, constituted of almost pure blood, either red and fluid or dark and coagulated. They may be muco-bilious or purely bilious; in the latter case they contain mucus in small quantity and are a little more abundant and fluid; in both cases they are more or less greenish, and microscopic examination reveals the presence of a small quantity of blood. At other times the dejecta lose their viscous character, become more watery and abundant, and are constituted by a serous or sero-sanguinolent liquid; they are of a reddish or brownish color and resemble meat-washings; floating about in them is found a shreddy and finely divided material of a grayish or reddish-brown color.

When the evolution of dysentery is complicated with gangrene, the stools assume a special gangrenous aspect; they are serous, of a dark brown or reddish-brown color, and contain in addition to finely divided membranous threads, larger and thicker masses of necrotic tissue of a grayish or black color; fragments resembling flesh are also found in them, infiltrated with blood and pus. The gangrenous dejecta have an unbearably offensive odor, sometimes resembling the smell of a corpse; and by this odor alone it is often possible to make the diagnosis of gangrenous dysentery.

Amœbæ are almost always found in every variety of dysenteric stools, in every period of the disease, being usually most frequent in cases in which the lesions are most extensive.

The secretions of the small intestine are almost always modified from the beginning of the disease, whether the secretory derangement is one of the consequences of the general intoxication, or, as is more probable, it is provoked by reflex irradiations whose starting-point is in the colon. The bilious secretion suffers also; during the premonitory stage bilious vomiting and motions are sometimes observed; then there is, so to speak, a suspension of the bilious excret-

ing function; the muco-sanguineous stools in many cases do not contain a trace of bile. In some patients a subicteric coloration of the sclerotic is observed, and the chemical examination of the urine reveals the presence of biliary pigment; it seems that in these cases there is stasis and reabsorption. The acholia and stasis are often interrupted by abundant bilious fluxes which modify the character of the dejecta, rendering them bilious, muco-bilious, or sero-bilious.

One of the most frequent and important symptoms of acute dysentery is the *abdominal pain;* it may even be said that it exists in all cases, with greater or less intensity. Usually the pains are felt as colic or intermitting tormina when there is a call to stool; these pains begin about the umbilical region and extend downwards, acquiring greatest intensity in the left iliac fossa; after the evacuation they diminish and cease. In the most severe cases, or those of medium intensity, they are frequent and come on independently of a desire to go to stool, when the patient moves about in the bed, or even spontaneously. These abdominal pains are sometimes so violent that the patient has to lie still, for fear of their being intensified by the least movement; he maintains a dorsal position and relieves all his necessities in the bed. The pains are sometimes localized about the abdomen, in the right hypochondrium, below the liver, in the right iliac fossa, in the umbilical region; in most instances, however, they are seated on the left side, along the tract of the colon and in the left iliac fossa; sometimes they are generalized throughout the abdomen. Pressure exerted on the large intestine provokes more or less intense pain; all the tract of the colon may be painful. In mild cases pressure with the fingers excites pain only when made in the left iliac fossa. During the periods of intermission of the diarrhœal flux the spontaneous pains diminish and disappear to return with exacerbation; often, even during the intermissions, strong pressure exerted on the colon excites violent pains. In gangrenous dysentery the pains, which are intense at first, go on decreasing as the disease progresses, and disappear when the destruction of the mucosa is complete; pressure may then elicit few or no signs of suffering. According to Dutrouleau, in some very grave cases there may be a total absence of colic from the beginning of the disease.

Another important symptom of dysentery, and one which is exceedingly annoying to the patient, is the rectal *tenesmus;* it consists at first in a painful sensation of pressure and constriction, accompanied by imperious calls to stool and extraordinary efforts, which bring about the expulsion of a small quantity of fæces. In grave cases the tenesmus consists in a special sensation of intense pain, spasm, and drawing that the patient feels in the anus; to the painful

spasm is added in some cases paralysis of the sphincter and the levator ani; the orifice remains open and the straining and tenesmus become almost continuous; the efforts to stool may cause prolapse of the mucosa. The tenesmus varies considerably in intensity in different patients and even in the same patient from one day to another; as a rule, the smaller the quantity of fæces evacuated the more intense and unbearable is the tenesmus; when a saline purge is administered, the dejections becoming more abundant and fluid, the tenesmus diminishes considerably. According to Dutrouleau, in the torrid zone the tenesmus is often wanting, or when existing has a passing duration, and there may be a burning sensation instead. Councilman and Lafleur confirm this statement. In Brazil the tenesmus is frequent,

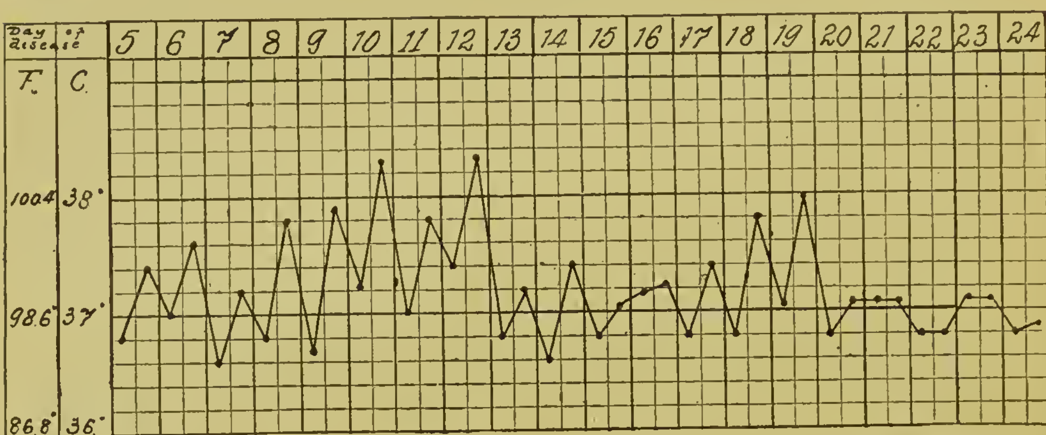

CHART No. 1.—Representing the Temperature Curve in a Case of Dysentery of Medium Intensity.

at least, I have never failed to observe it in a single case of acute dysentery. In grave cases the tenesmus extends to the neck of the bladder and is accompanied by dysuria or even strangury. The condition of the patient then becomes pitiable; the straining is often agonizing and provokes cries, a convulsive tremor of the limbs, and sometimes fainting.

The tenesmus, the abdominal pains, and the particular nature, already described, of the alvine dejections constitute the cardinal symptoms of dysentery; to these are to be added many others which are less constant or which vary in different cases.

In many cases, chiefly in times of epidemic, the disease begins with cold chills and *fever;* the latter is never very high unless there are complications, and ceases at the end of two or three days. In mild cases fever is rarely observed in the course of the disease; in cases of medium intensity, however, there is always a slight increase of temperature (37.5°–38° C., 99.5°–100.4° F.), coming on generally in the afternoon; the feverish condition is aggravated when the diar-

rhœa and the tenesmus grow worse or when the liver is involved (hyperæmia or abscess). The variation of temperature and the type of the fever are always irregular. The accompanying chart shows the progress of the temperature in a case of medium intensity observed by me in January of this year, and terminating in recovery.

Sometimes, at the beginning of the disease, there is *gastric derangement* with loss of appetite, nausea, vomiting, foul tongue, painful tension of the epigastrium, etc. In mild cases the appetite is often retained and the gastric functions are performed perfectly well. In severe cases, or in those of medium intensity but of long duration, there is more or less accentuated anorexia, great thirst, and the tongue is sometimes covered with a white coat, and is sometimes red and irritated. Vomiting may come on every now and then, almost always coinciding with the administration of medicines or the taking of food.

The *urine* is scanty, of acid reaction, and of high specific gravity, with an excess of urea and uric acid and a diminution of the chlorides; sometimes it contains biliary pigment. In cases of medium intensity the urine is slightly albuminous, and in severe cases a chemical examination reveals the presence of indican and a sensible reduction of urea.

In many patients a careful examination of the *liver* during the whole evolution of the disease reveals nothing abnormal; in some patients, however, an increase in the volume of the liver may be observed at any period of the disease, accompanied with spontaneous or provoked pain in the region of the organ, and with an elevation of temperature; these symptoms are sometimes preceded by slight chills, and indicate the existence of hepatic congestion or of hepatitis, which will terminate by resolution or by the formation of an abscess.

In mild cases the *general condition* is little changed; the nutrition is not much impaired, the patients merely complaining of slight muscular weakness and loss of flesh. The decubitus is indifferent, the pulse is about normal, the appetite is retained or slightly diminished. In grave cases, or in those of medium intensity but of prolonged duration, there are more or less rapid loss of flesh, more or less accentuated prostration, dryness of the skin, alteration of the features, cold extremities, exaggerated sensibility to cold, weakening of the contractile energy of the myocardium, loss of strength, and vertigo. The pulse is small and rapid; the patient remains in the dorsal decubitus with limbs extended, the belly being retracted and exceedingly painful. In certain grave cases these symptoms are still more accentuated; the calorification and nutrition are greatly impaired, and

algor manifests itself among other symptoms that remind one of Asiatic cholera. At other times the typhoid syndrome predominates; cerebral disorders are then observed—delirium, at first nocturnal and afterwards continued, stupor, drowsiness, sudden jerkings of the tendons, carphologia, hiccough, general and extremely pronounced adynamia, dry and dark tongue, abdominal meteorism, etc. In other cases hemorrhages constitute the principal feature—grave and multiple hemorrhages seated in the intestine, the other mucosæ, the skin, and the cellular tissue. Sometimes in grave cases the clinical scene is modified by a train of new symptoms which indicate that the peritoneum is involved: the temperature rises, the belly is rounded, tympanic, and exceedingly painful, and there is more or less frequent vomiting. In other exceptional cases we find suppurative inflammation of the parotids, abscesses in various parts, eschars of the sacrum, and in fact, all the symptoms of septicæmia.

Course and Duration.

The course of acute dysentery is not always the same in all cases; it may be continuous and ascending, the disease growing constantly worse until a fatal termination; it may be continuous and at first ascending, the symptoms growing slowly worse, and then abating until a final recovery; the disease may also present itself from the first with marked gravity and then go on yielding little by little until a complete cure; finally, the course may be discontinuous, with periods of intermission and aggravation.

The duration of acute dysentery is very variable; a cure is effected in some cases within from eight to fifteen days; in others the disease is prolonged for a month or even more, passing into a subacute and chronic state; in other cases death may occur at the end of seven or eight days. A dysentery at first mild, with intermissions and exacerbations, may terminate in death, the grave precursory symptoms of the fatal termination lasting two, three, four, or five days.

Varieties.

The clinical aspect of acute dysentery varies considerably by reason not only of individual circumstances, but of extrinsic conditions as well. This variability refers to the manner in which the symptoms are grouped, their order of succession, their greater or less intensity, the rapidity of the evolution of the disease, and the unusual gravity of certain cases contrasting with the recognized mildness of others. For greater facility of diagnosis, observers of all times have described various clinical forms, taking for a basis the predominant symptoms. The following forms have been admitted: simple, in-

flammatory, bilious, catarrhal, rheumatic, phlegmonous, hemorrhagic, typhoid, gangrenous, algid, choleraic, etc. The symptomatic predominance does not seem to me a solid and convenient basis for a good classification of cases; besides permitting the description of numerous clinical forms, which renders the diagnosis difficult, it must be added that these forms are very unstable, since in the same patient the symptoms that predominate one day may be replaced by others the next day, and so on. I prefer, after the example of Dutrouleau and Kelsch and Kiener, to classify the cases according to the degree of gravity of the disease, taking the morbid ensemble into consideration. I shall describe for acute dysentery three forms: the mild form, that of medium intensity, and the grave form, each one of them admitting clinical varieties which may be characterized by the predominance of some symptoms.

In the *mild form*, the clinical ensemble is almost exclusively taken up with local symptoms which in general are not very intense. With or without the precedence of premonitory symptoms, the disease begins by diarrhœa, which may or may not be accompanied with colic, foul stomach, nausea, and loss of appetite; the dejecta are fluid or fecaloid, differing little from those of simple diarrhœa. At the end of the first or second day the stools assume a dysenteric character; they become more and more frequent and less abundant and are frankly mucous or sanguinomucous; the patient complains of colic and tenesmus; the latter may in the simplest cases be limited to a sensation of heaviness and burning in the anus. The patient has from six to ten dejections a day; he feels pain only when he has a call to stool; the colic, preceded by borborygmi, nearly always begins at the navel and extends over the left side, being most accentuated about the left iliac fossa. The general symptoms, when they exist, are limited to an exaggeration of sensibility to cold, weakening of the muscles, and vague pains in the members and articulations. The patient does not keep his bed, and frequently continues to busy himself with his habitual occupations. At the end of six, eight, or ten days in some cases, the dejecta, owing to the treatment instituted or even in the absence of any treatment, begin to suffer modification, becoming more abundant, more feculent, and less frequent; the colic diminishes in intensity, the tenesmus gradually disappears, and the patient recovers. At other times the disease presents intermissions and exacerbations; the patient during one or more days has one or two feculent dejections, without colic or tenesmus; then comes on, rapidly or slowly, a period of exacerbation, characterized by frequent small sanguinomucous dejections with colic and tenesmus. The disease may thus last for twenty days, a month, or longer,

terminating in recovery or passing into a chronic state. At other times there is an alternation of diarrhœa and constipation; after a few days of frank dysentery the patient passes one, two, or three days without an evacuation; he eats with a good appetite and imagines that he is nearly well; then comes on, either spontaneously or provoked by a purge, a diarrhœa which lasts three or four days; the first stools are watery and abundant, and attended with little pain; those which follow, however, are frankly dysenteric, frequent, diminished in quantity and mucosanguinolent, and attended with violent colic and tenesmus; this period of diarrhœa is followed by another of constipation, and so on, until the disease terminates in recovery, passes into a chronic state, or is modified in its evolution by an acute and grave recrudescence of the symptoms or an accident leading to death.

The form of medium intensity is characterized by more accentuated local symptoms, by general symptoms, by the nutrition being more seriously deranged, and by a greater gravity, the disease being liable to terminate fatally. It may or may not be preceded by premonitory symptoms; it commences usually at night with violent colic and frequent stools; sometimes it comes on after exposure to cold, a suppression of perspiration, or an indigestion, and is accompanied by light chills and fever. The first fluid and fecaloid dejections contain a little mucus and blood; they soon become diminished in quantity, being mucous, mucosanguinolent, or frankly bloody; they occur from fifteen to twenty-five times a day, and are accompanied by violent colic and tenesmus. Abdominal pains, either spontaneous or provoked by any movement, are felt; the patient keeps his bed and maintains the dorsal decubitus. The skin is alternately cold and hot, dry and damp; the pulse is frequent and small. During all the evolution of the disease there may be no fever; at other times the fever which accompanies the initial symptoms lasts only one or two days and ceases, not to return; in the majority of cases, however, the patient complains of a slight febrile movement, the temperature oscillating between 37° and 38.2° C. (98.6° and 100.7° F.). The abdominal pains sometimes provoke vertigo, and the tenesmus may extend to the neck of the bladder, producing dysuria. There is no appetite, the emaciation becomes more accentuated every day, and the patient complains of great prostration and muscular weakness. The disease may last in this manner for ten, twelve, or fifteen days; the pains then abate, the dejecta begin to suffer modifications, the tenesmus disappears, and after a few days more the appetite reappears and convalescence sets in; this is always of long duration. Recovery may be interrupted by a short and temporary

return of the dysenteric flux. In some cases the disease terminates fatally; at the end of twelve or fifteen days the patient is much weakened and very anæmic, and death occurs in consequence of a syncope, of a hemorrhage, or of a general weakness and collapse. This termination is observed when the dejections have been frankly bloody during several days consecutively; they are then constituted by pure blood, mixed with small black clots, which the patient expels with great effort, violent pains, and intense tenesmus. This clinical variety of dysentery is frequently observed in Brazil, especially during epidemics, and is known in the interior of the country by the name of *camaras de sangue.*

Acute dysentery of medium intensity does not always exhibit the continuous course I have described; in many cases successive intermissions and exacerbations are observed. The periods of intermission are ordinarily very short; they last from eight to thirty-six hours; frequently the periods of intermission and exacerbation present so much regularity as to remind one of the manifestations of malaria; during several successive days, for instance, the patient passes the morning very well; until one or two o'clock in the afternoon he has no evacuations and the pains are slight, he is able to take some nourishment and sleeps calmly; from two o'clock on and during the greater part of the night he is worse, passing frequent motions accompanied with violent pains and tenesmus, and having calls to stool at every moment; he lies as still as possible in bed in order to avoid the aggravation of the pain excited by the least movement. A slight fever often accompanies the exacerbations, and the temperature is then frequently intermittent.

The *grave form* of acute dysentery may be primary or secondary, that is, it may begin as such abruptly from the commencement of the disease, or it may develop during the course of a mild dysentery or one of medium intensity. This last mode is observed in the majority of cases; the invasion of the severe form is then announced by fever, more or less intense pains, agitation, change of the nature of the dejecta, etc. Primary grave dysentery is almost exclusively observed in times of epidemic; it is often preceded by premonitory symptoms, a general bad feeling, prostration, loss of appetite, foulness of stomach, and constipation or slight diarrhœa. The symptoms characteristic of dysentery appear in an abrupt manner; the patient is taken with intense colic in the hypogastrium or over the colon; he frequently has chills, and fever which is never higher than 39° C. (102.2° F.). He has calls to stool at every moment, and after great effort and intolerable tenesmus he succeeds in expelling a small quantity of mucosanguineous matter. The calls to stool are repeated

with extraordinary frequency; he has forty, sixty, eighty or more dejections in the course of twenty-four hours; in some patients the calls to stool have been known to be repeated more than twenty times in an hour; the patient no sooner leaves the closet than an imperious call accompanied with griping pain obliges him to return. The skin is alternately hot and cold, the pulse is frequent and small, the patient complains of great depression and loss of strength; sometimes there is fainting after intense and vain efforts to evacuate the bowel. These symptoms go on growing worse, the general condition of the patient becoming aggravated; the fever persists, oscillating irregularly between 38° and 39° C. (100.4° and 102.2° F.); the dejecta are alternately mucosanguineous, bilious, or frankly bloody. At the end of four, five, or six days new symptoms indicate the appearance of intestinal gangrene. The motions become watery, of a reddish-brown or dark-brown color, like the washings of meat, and of a cadaverous odor. On examination they are found to contain membranous shreds and sloughs of varying size, often infiltrated with pus or blood. The fragments of mucous membrane found in the stools may be so small as to be detected only by careful search, but they are often of considerable size. Fayrer relates a case in which a tubular slough about a foot long was discharged; Dutrouleau publishes the observation of a case of gangrenous dysentery with the expulsion of a portion of the intestinal mucosa 35 cm. (14 in.) long; the patient recovered. The expulsion of these long portions of disintegrated membrane is ordinarily announced by a violent vesical tenesmus and great dysuria.

The motions are repeated with great frequency; the sphincter ani is paralyzed, the anus open, and the mucosa prolapsed; the urine is diminished and chemical analysis reveals the presence of albumin or of indican; there are intense thirst and great anxiety. The *facies* of the patient is greatly altered, the features are haggard, the nose is thin, the eyes are sunken, the skin of the face is parchment-like; the belly is depressed, hollowed, and very sensitive to pressure. The pulse is small and irregular; the cardiac sounds are dull, almost imperceptible; the breathing is short and interrupted by heavy sighs; sometimes there is hiccough. The temperature goes on gradually decreasing; the coldness begins at the extremities and advances to the trunk; a cold sweat covers the whole body; the voice is extinguished and the patient dies in a state of collapse and algor, almost without agony, retaining complete intelligence and sometimes a sense of approaching death. Sometimes muscular cramps are associated with the algor as well as copious fluid motions of a dark color and a gangrenous odor, suppression of urine—in fact, an ensemble of symptoms

similar to those of Asiatic cholera. When the gangrene of the intestine is extensive the horrible pains felt at the onset of the disease frequently cease or abate, and pressure on the abdomen may then cause little or no suffering.

During grave epidemics, patients are sometimes observed with symptoms somewhat different from those I have just described. Sometimes the morbid scene is almost wholly taken up with repeated hemorrhages, bloody stools, epistaxis, petechiæ, stomatorrhagia, etc., accompanied by violent colic and tenesmus, great prostration, fever, sometimes cold extremities, smallness of pulse, fainting, and death in a state of collapse. Sometimes the predominant symptoms are typhoid—frequent evacuations of a dark color and very fetid odor, fever of a continuous or remittent type, dry tongue, sordes, fetid breath, carphologia, hiccough, dyspnœa, and meteorism.

Chronic Dysentery.

The chronic state is often established after various repeated attacks of acute dysentery, these attacks being either distinct repetitions separated by intervals of complete recovery or true relapses, the patient not having regained during the intermission the structural integrity of the intestine. At other times chronic dysentery succeeds one of the mild or grave forms of the acute process, continuing it with attenuated symptoms; when the chronicity is established, the general symptoms gradually abate, only the local ones remaining. Finally chronic dysentery may begin insidiously with a simple or indolent diarrhœa; at the end of a few weeks and after alternations of improvement and aggravation, the dejections are found during the exacerbations to contain mucus and blood, and are then accompanied with tormina and straining; the disease continues with longer or shorter stages of intermission and exacerbation, and chronic dysentery is established.

When chronic dysentery has set in, the symptoms succeed each other in various ways according to the cases; these may be classified in three groups, which correspond to the three clinical forms: the very mild form, the moderately severe form, and the severe form.

In the *mild form* the disease sometimes passes almost unnoticed, so insignificant and faint are the symptoms indicative of it; the patient complains merely of habitual constipation of the bowels, interrupted by transitory diarrhœas, without either colic or tenesmus; during the periods of diarrhœa, the watery and feculent motions contain mucus and a little blood, and pressure exerted on the cæcal region or the left iliac fossa elicits a dull pain. At other times the

patient has a characteristic dysenteric flux which lasts four or five days; he has five or six motions a day, at first watery and afterwards diminished and mucosanguineous, accompanied with violent colic and tenesmus; he gets on perfectly well during fifteen or twenty days, having only one dejection per diem and eating well. At the end of this time, either spontaneously or from some trifling cause, such as a cold, a digestive derangement, etc., the dysenteric flux returns, ceasing at the end of from three to five days, to return again after a period of apparent good health, and so on successively. I observed a case of this nature with a duration of over twenty years; it was that of a lady sixty-two years of age, strong and stout, whose looks denoted excellent health; she complained of a mucosanguinolent diarrhœa with colic and tenesmus, which lasted four or five days, and came on every month; during the intervals she got on very well. At the beginning, the diarrhœa coincided with a somewhat premature suppression of the menstrual flow, at the age of forty years; she did not choose to undergo treatment, being convinced that it was a supplementary derivation of blood; by the advice of a physician she merely took a strong dose of paregoric elixir on the fourth day of the disease and so succeeded in stopping the diarrhœa. In the fæces of this patient, microscopical examination made by Prof. Chapot Prevost revealed the presence of amœbæ in active motion.

In the *form of medium intensity* there are loss of appetite and emaciation; the disease almost always presents itself with phases of intermission and exacerbation. The periods of intermission last from four to ten days; during them the patient may have constipation or he may have one or two evacuations a day, the stools being feculent and soft and containing little mucus. The stages of exacerbation last four or five days or longer; the motions become more watery and contain mucus and a little blood, being accompanied with some colic and sensation of heat and burning in the rectum. It is not uncommon that the patient during several successive days passes the day well, but during the night has three or four watery dejections containing mucus and blood and accompanied with colic.

In the *severe form* the general nutrition is greatly impaired; the emaciation is pronounced; the appetite is lost, the digestion is difficult, the tongue is foul, the pulse is weak and frequent. There is vomiting once in a while; the belly is depressed, hollowed, and painful to pressure; the skin is generally dry and the urine is diminished in amount. The character, consistence, and frequency of the dejections vary greatly in the same patient from one day to another. They may be diminished, mucous or mucosanguineous, and frequent, the patient going to stool four or five times in the course of the twenty-

four hours; they are then accompanied by tenesmus and more or less violent colic. They may be more watery and feculent, being repeated two or three times a day without either colic or tenesmus. They may be lienteric, fragments of undigested food being found in them. Finally, in some cases the diarrhœa alternates with constipation, which lasts two or three days. After some time, the emaciation is accompanied with pronounced anæmia. Œdema of the feet and legs is then observed. The strength of the patient is greatly impaired; he keeps his bed and finally dies in consequence of the marasmus and cachexia, or by the supervention of an accident, such as hemorrhage, abscess of the liver, peritonitis, or by reason of an acute exacerbation of the dysenteric process accompanied with gangrene of the intestine.

The duration of chronic dysentery is counted by months and years. When not submitted to proper treatment the disease tends to grow worse as time goes on. Thus we not infrequently see a very mild form change into a moderately severe form, and the latter afterwards assume the clinical characters of severe chronic dysentery.

Complications and Sequelæ.

Peritonitis.—Peritonitis is one of the most frequent complications in the course of acute dysentery; it may result from the propagation of the phlegmasic process from the intestinal tunics to the peritoneum in the neighborhood of the ulcers, or it may be the consequence of a perforation. In the first case, the peritonitis is commonly partial, being localized around its point of origin; it nearly always passes unnoticed during life. In the second case the peritonitis is generalized, acute, and very grave. The perforation of the intestine is most frequently observed in gangrenous dysentery; its seat is variable; according to Bérenger-Féraud it occurs in the rectum, in the sigmoid flexure, or in the descending segment of the colon. When the perforation of the serous coat supervenes, the temperature rises, the belly becomes rounded, tympanic, and excessively painful, and more or less frequent vomiting comes on; the pulse is weak and frequent, the skin is covered with sweat, and the patient dies in collapse. It is not exceptional to observe sudden death consecutive to a perforation of the serous coat.

Hemorrhage.—In some cases of acute or chronic dysentery an abundant hemorrhage of the intestine may be observed; when it supervenes in an individual already weakened by former losses or by many days of disease, death may result from it, the patient dying in a collapse.

Rheumatism; Arthropathies.—The physicians of the eighteenth century signalized, among the symptoms of dysentery, articular fluxions and rheumatism. This traditional notion found full support in the authority of Trousseau, who described a rheumatic form of dysentery. Cambay, Quinquaud, Dewevre, Dutrouleau, Delioux de Savignac, Bérenger-Féraud, and others formally admit a relation of cause and effect between dysentery and the arthropathy which sometimes supervenes in its course. The articular symptoms may be observed during the evolution of acute dysentery during the first or second week; ordinarily, however, they appear during convalescence. In some cases it is a polyarticular rheumatism, accompanied or preceded by vague pains in the limbs or muscular pains, either fixed or generalized; this rheumatism runs its course concomitantly with the dysentery, disappearing with it or before it. In other cases the rheumatic affection is stubborn, being fixed from the start in one single articulation; or, as happens more frequently, it is localized in one or two, after having affected successively the others. This arthropathy develops as a rule during convalescence; it may also be observed during the evolution of the disease, coinciding with a suppression of the dysenteric flux. The pain is dull, without exacerbations; the local temperature is not modified, the teguments retain their normal coloration; the periarticular tissues become tumid. The presence of liquid has rarely been observed in the synovial sacs. Notwithstanding its slow and prolonged evolution, the prognosis of the arthropathy is favorable, as it always terminates without ankylosis and without suppuration.

I have never had occasion to observe the articular symptoms of dysentery, which leads me to accept the opinion of some authors who assert that they are much more frequent in the dysentery of temperate and cold climates.

Thrombosis.—In a work published in 1885, Laveran relates three cases of femoral thrombosis and one of thrombosis of the venous sinuses of the brain, developed either in convalescence from an acute severe dysentery or during the course of chronic dysentery. Cambay related an instance of thrombosis of the left iliac artery with gangrene of the corresponding member. Other cases more or less similar are registered in medical literature, but they are yet in too small a number to permit of forming an exact opinion on the subject.

General Dropsy.—Haspel, Canteloup, and Cambay mentioned among the sequelæ of dysentery a general and considerable anasarca, developing in a rapid manner during convalescence from acute grave, or in the course of chronic, dysentery. Dutrouleau and Delioux de Savignac saw dropsy become much rarer after the recasting

of the therapy of the disease, which before that was based on the teachings of Broussais, and this inclines one to the belief that that symptom was rather a consequence of abundant blood-letting than of the dysentery itself. The study of the pathological conditions and of the pathological physiology of this disease shows us that dropsy is exceptional in the acute form and tardy in the chronic form, and attains a high degree of intensity. Indeed, it is limited to the malleolar region, and disappears with rest or persists for a long time without any tendency to generalize. In some rare cases small effusions in the serous cavities are observed.

Hepatitis and Abscess of the Liver.—Of the complications of dysentery the most frequent, and incontestably the most important, is hepatitis, which may terminate in resolution or in suppuration. Dysenteric hepatitis is rare and exceptional in cold and temperate climates; it begins to be observed oftener in the subtropical regions, and its frequency increases progressively towards the equator. Hepatitis may precede, follow, or accompany dysentery; in the majority of cases the abscess of the liver is observed in convalescence from acute dysentery or during the evolution of chronic dysentery. It may develop in a dysentery of any degree of severity and at any period of the disease; ordinarily, however, it is observed in mild forms and those of medium severity of acute dysentery when prolonged, and in chronic dysentery. In Brazil, where tropical abscess of the liver is very prevalent, I have never observed it in the grave forms of acute dysentery. It may, likewise, develop as a primary affection, being followed or not by dysentery. When hepatitis develops in the course of acute or chronic dysentery it is not uncommon to observe a sensible diminution or even the complete disappearance of the dysenteric symptoms, or the substitution of a mucosanguineous flux by a simple diarrhœa or by constipation.

The *symptoms* of dysenteric hepatitis vary greatly in individual patients, the symptomatological ensemble often presenting itself totally different in two persons observed at the same time and in the same endemic centre. The irregularity of evolution, with an alarming or insidious onset, with exacerbations, remissions, relapses, and a tendency to chronicity, and the inconstancy of the symptoms impressing different clinical features according to the cases, are the fundamental characters of dysenteric hepatitis, the lines which predominate in its clinical history. Sometimes it evolves rapidly and tumultuously, terminating in a few days with the opening of a focus of suppuration on the outside or in a neighboring cavity; sometimes essentially slow and insidious, it takes weeks and months to complete its evolution; in certain cases it is denoted by a classical train of

symptoms which greatly facilitate the diagnosis; in other cases it defies the sagacity of the practitioner, confusing him completely, even if it does not produce an autopsy surprise.

At the beginning hepatitis is ordinarily announced by chills, fever, pain in the right hypochondrium, and increase in size of the liver. The pain is sometimes mild, increasing under pressure or with the great respiratory movements; at other times it is violent, intolerable, and radiates to the right shoulder or to the abdomen. The febrile movement may be slight, not exceeding 38° C. (100.4° F.); rarely does the thermic curve go beyond 39° C. (102.2° F.); the fever presents the remittent or subcontinuous type. In some cases, besides these symptoms, there are foulness of the tongue, nausea, bilious vomiting, slight jaundice, sleeplessness, and prostration. These symptoms persist for two, three, four, or five days, and if the hepatitis terminates in resolution a rapid and sensible improvement is observed at the end of that time: the fever ceases, the pain diminishes without disappearing entirely, and the liver tends to acquire little by little its normal dimensions. At other times the symptoms, after attaining their maximum intensity, abate slowly and gradually, being then repeated in the form of paroxysms, but do not disappear definitely until after several relapses, leaving behind a more or less persistent tumefaction of the liver. When the hepatitis tends to terminate in suppuration, after one or more congestive attacks at the climax of one of the paroxysms, the symptoms persist with modifications and association of new ones, which indicate the formation of the hepatic focus. Nevertheless, the abscess may be formed insidiously and only be manifest clinically later on, when it acquires great volume; after the first congestive attacks, the patient supposes he is cured and he goes about his habitual occupations, feeling only a slight sensation of heaviness in the right hypochondrium; after a great many days, when the purulent focus is formed and has reached a large size, the diagnosis may be arrived at by the help of certain symptoms. I have observed two cases in which the affection presented these characters.

Pain is one of the symptoms persisting after the congestive period of hepatitis, remaining in most cases during the whole evolution of the process. Its seat, intensity, duration, and time of appearance vary greatly. The seat of the pain is usually that of the lesion; it is felt on the level of an intercostal space, in the epigastrium, below the costal edge, in the depth of the hypochondrium, or in the renal region, according as the abscess is localized on the convex surface of the right lobe, on the left one, on the concave face, or at the posterior edge of the liver. It may be circumscribed to one or another of these

points, or it may be generalized over the whole of the hepatic region. In some cases it acquires from the beginning its maximum intensity; in others, having commenced as a mere feeling of heaviness, it goes on gradually increasing. Its degree of intensity is usually dependent upon the seat of the abscess; if weak, vague, without a precise seat, it indicates a central focus; if acute, violent, radiating to the upper part of the abdomen, it denotes a superficial focus in connection with the peritoneum. The radiation of the pain to the right shoulder is commonly observed in abscess of the right lobe of the liver, which is the most frequent. The scapulalgia, without having, as some have maintained, a pathognomonic value, constitutes an important element of diagnosis.

During the hyperæmic or presuppurative stage of dysenteric hepatitis, the liver acquires great volume, but diminishes sensibly as soon as it is over; then, as the pus forms and collects, the organ again increases, and the increase is more or less in relation to the extension, volume, seat, and number of the abscesses. In abscesses of the right lobe the superior limits of the hepatic dulness rise considerably; the lung is pressed upwards, and the movements of the diaphragm are embarrassed; hence the oppression and dyspnœa that the patients complain of, not infrequently accompanied with a dry clear cough, similar to pleuritic cough, and owing, no doubt, to an irritation of the diaphragmatic pleura.

The hepatic complication of dysentery may develop without fever; the fact is exceptional, and in the majority of cases there is a frank febrile movement. The fever may exist without interruption, suffering only a modification of type from the presuppurative stage of the hepatitis. At other times there is between the stages a period of complete apyrexia. In the first group of cases it assumes at first the remittent type, with evening exacerbation; afterwards the fits of fever become frank and are separated by intervals of apyrexia, being repeated a great many times in the same day; each fit is preceded by slight chills and terminates with sweating and prostration; the attacks present in their course, duration, and periodicity great irregularity. Finally, the patient may have only one paroxysm during the day, and this being daily repeated at certain hours, reminds one of a malarial fever. In the second group of cases the fever generally assumes the intermittent type; the temperature seldom exceeds 39° C. (102.2° F.); the attacks are usually preceded by rigor and slight chills, terminating in abundant, cold, clammy sweats.

Jaundice is rare, and when it exists it is light, being limited to a slight yellow coloration of the skin, which is more accentuated in the nasolabial furrow and on the sclerotic.

The course of tropical abscess of the liver is very irregular and capricious; sometimes the affection progresses rapidly and tumultuously, the symptoms growing worse from day to day, denoting a continuous and uninterrupted progression of the disease; at other times the progress is interrupted and paroxysmal, with intermissions and exacerbations; in this last case the disease consumes weeks and months before terminating its evolution. Abandoned to itself, without therapeutical intervention, the large abscess of the liver terminates in most cases in death. This may be the consequence of complete exhaustion, the general nutrition being impaired to an irreparable degree, the forces of resistance being gradually annihilated, and cachexia setting in. Sometimes death is due to a superacute recrudescence of the dysenteric flux; in the majority of cases, however, it results from the opening of the focus of suppuration in a neighboring cavity, and from the inflammatory phenomena brought about by it. This irruption of the contents of the abscess through a neighboring cavity does not always result in the death of the patient; sometimes it hastens the evolution of the disease to a favorable termination. Recovery may also follow the opening of the focus through the cutaneous tegument.

Of all the modes of spontaneous termination of suppurative hepatitis, that which is most frequently observed is the opening of the focus in the bronchia or in the pleura, which is explained by the greater frequency of the abscesses on the convex face and posterior edge of the liver. When the contents of the abscess flow into the interior of a bronchial cavity, the patient presents the symptoms of a more or less intense inflammation at the base of the right lung. The quantity of matter expectorated varies from 100 to 300 gm. (3 to 10 ounces) in twenty-four hours, and sometimes reaches 700 gm. (22 ounces); it presents a chocolate color and is mixed with white mucous detachments and yellowish purulent streaks. This expectoration persists during several weeks and even months, with variable alternations, and is always accompanied with violent coughing. When the contents of the abscess flow into the pleura, the patient presents the symptoms of pleurisy with effusion. The abscess may also empty itself in the mediastinum, in the pericardial cavity, in the peritoneal cavity, or in one of the segments of the digestive tube, from the stomach to the colon, including the biliary ducts. These various modes of termination of suppurative hepatitis, formerly observed with great frequency, are now growing more and more rare since the elements of diagnosis have become more precise; it may be asserted to-day that the great majority of cases of tropical abscess of the liver terminate with the evacuation of the focus by the surgeon.

Paralysis.—Among the complications and accidents observed in the course of chronic dysentery and in convalescence from acute dysentery, are worthy of special mention the various forms of paralysis which have been signalized and described by different authors. In 1860 Gubler, collecting the cases in medical literature which were entirely free from doubt, was able to publish only three—one of Moutard-Martin and two of Duroziez. In 1867 Delioux de Savignac related two cases; two years later Leyden published two more cases, and, analyzing the symptoms, said that the starting-point of the accident was an ulceration of the sigmoid flexure caused by an ascending and descending neuritis of the sacrolumbar nerves propagated to the rachidian meninges. In 1885 Laveran related another case; in 1888 Pugibet collected seventeen observations, of which seven were his own; finally, in 1897, Bonardi published a case, terminated by death, and described the lesions found.

Up to the present time I have had the opportunity to observe only one case of paralysis developed in convalescence from acute dysentery, and am not aware that this complication has been observed by other physicians of Rio de Janeiro, which leads me to believe it is extremely rare. In my patient the morbid phenomena predominated in the lower members; there were pronounced motor paresis, abolition of the reflexes, exaggerated painful sensibility; in the upper members the patient complained only of numbness and a pricking sensation in the fingers.

In Bonardi's patient, besides the more or less accentuated weakness of the four members, there were disorders of general sensibility with separation of its various forms, reaction of degeneration, and œdema of the lower members. The post-mortem examination showed the absence of medullary lesions and well-marked alterations in the peripheral nerves, chiefly the radial, musculocutaneous, tibial, and peroneals.

According to Pugibet, the pathogenic condition of post-dysenteric paralysis consists in a capillary thrombosis of the anterior segment of the medulla. Leyden is inclined to accept a local starting-point for the paralysis, considering it the result of an ascending and descending neuritis, originating in the ulcerated intestinal mucosa. It is possible that the cases of painful paraplegia developed during the evolution of dysentery or at the beginning of convalescence, and whose first symptoms have the lumbar and sacral region for their seat, obey this pathogenic condition. The explanation of Leyden cannot, however, be accepted in relation to tardy paralyses, appearing at the end of convalescence and after the cure of the local process, or located at points which have no anatomical connection with

the intestinal nervous plexus. It seems to me more reasonable to admit in these cases a specific action exerted on the peripheral nerves or the neurons, bringing on the development of cases of neuritis and polyneuritis more or less similar to those observed in convalescence from certain infectious diseases—smallpox, diphtheria, typhoid fever, tuberculosis, etc.

Diagnosis.

The diagnosis of acute dysentery is ordinarily easy, and in order to establish it it is sufficient to pay attention to the symptoms by which the disease is commonly expressed. It might at first sight be confounded with a simple diarrhœa, a tuberculous enteritis, a mucomembranous enteritis, a toxic enteritis, cholera nostras, etc. To distinguish it from these various affections it is sufficient to attend to the character and nature of the motions, to their number, to the colic, to the tenesmus, the painful points along the tract of the colon, and to the disorders of calorification and nutrition.

The diagnosis of chronic dysentery is sometimes delicate and difficult, chiefly in its mild forms, which are confounded with diarrhœa and other chronic enteritides. A minute and complete examination of the fæces is then necessary, and the presence in them of amœbæ in active movement is a valuable element in favor of dysentery. In many cases one single examination of the stools will be sufficient; in others, however, repeated examinations may be required. Besides this, great attention must be paid to the history of the disease. Cancer of the rectum, rectal polypus, and proctitis sometimes exhibit symptoms suggestive of chronic dysentery; in these cases, however, a careful and prolonged examination will remove all doubts.

The diagnosis of dysentery is occasionally also more or less difficult when new symptoms become prominent in the morbid scene, and those which commonly express the disease exhibit themselves modified in their intensity, in their evolution, in their grouping and succession. This is observed when, concomitantly with dysentery, there develops in the same patient another disease associated with it, they both, in their common action on the system, suffering modifications in their evolution and symptomatology which denote a reciprocal influence. The two associated diseases may furthermore strengthen each other during their course, or oppose each other in some of their clinical and anatomical manifestations. Facts of this nature have been remarked in all ages, and they even justify certain clinical forms admitted by some authors—the intermittent form, the scorbutic form, the rheumatic form, etc.

Dysentery may be associated with malarial fever, scurvy, rheumatism, typhoid fever, exanthematic typhus, cholera morbus, etc. Between the tropics the association of dysentery and malaria is very frequent. Pereira Rego, recording the epidemic that developed in Rio de Janeiro in 1864, writes: "A phenomenon commonly observed in the course of this epidemic, chiefly in the months of December and January, was the suspension of the evacuations during the day, and their return from nine or ten o'clock at night, this return coinciding with hot skin, burning thirst, rapid pulse, insomnia, and agitation; on undetermined days there were frank paroxysms entirely similar to those of periodical fevers. These attacks became very distinct about the seventh, eleventh, and fourteenth days of the disease, by reason of their termination in copious sweats, great depression, cold skin—in fact, all the symptoms similar to those of algid fevers. In these cases the use of strong doses of the salts of quinine usually brought the patient to convalescence or caused the dysenteric state to decline, modifying the character of the stools. This circumstance induces the belief that dysentery was associated with malarial fever."

Dysentery and malaria developing in the same person may not exert on each other any influence whatever; each commences and terminates at a different time, following its ordinary course during the period common to both. In other cases, being independent at their beginning and termination, they aggravate each other during the period of common evolution. Such is the case related by Gestin: An individual affected with dysentery of nine days' standing, and who was already in a fair way to recovery, had a violent malarial attack, which was repeated the next day; each attack was accompanied with a recrudescence of the dysenteric symptoms. Being treated with quinine, the attacks disappeared, but the dysentery persisted with increasing gravity, resulting in the death of the patient at the end of a few days. In another order of facts, malaria, instead of aggravating dysentery, seems to embarrass and even suspend its evolution, as in the following case, related by Dutrouleau: A person with an acute dysentery of seven days' standing was improving rapidly, when choleriform accidents abruptly supervened, algor, cramps, vomiting, etc.; on the administration of strong doses of quinine these symptoms disappeared, and the dysentery, suppressed during the algid paroxysm, did not reappear. Not infrequently dysentery is seen to begin in a frankly intermittent manner, with daily or tertian attacks, accompanied or not with febrile movement; or in a remittent manner with morning or evening paroxysms, accompanied or not with fever of the same type; on the administration of quinine the fever disappears, and the dysentery follows its normal evolution.

The association of dysentery with cholera has been noted in India in places where the two diseases have identical endemic centres. Dr. Victor Bigot observed three such cases; according to him, the dysentery was modified in its evolution; the dejecta lost their muco-sanguineous character and became watery, abundant, and whitish, without rhiziform particles. Vomiting, cyanosis, algor, haggardness of the features, and cramps supervened. Later, when the reaction set in and the choleraic accidents were over, the dysentery continued its course, regaining its normal character, though a good deal milder than before.

Typhoid fever may develop during convalescence from dysentery, and vice versa; in that case it will not be difficult to recognize the succession of the two diseases and determine the end of one and the beginning of the other. But in rare and exceptional cases they may begin at the same time, and influence each other reciprocally during their common evolution in the human organism. In support of this opinion we have the facts observed by Trousseau and Parmentier, by Bretonneau, by Morgagni, by Colson in the epidemic of 1853 in Ilet-la-Mère, by Erhel in Tahiti, by Kelsch and Kiener, and by Jules Perier in the epidemics in the camp of Châlons in 1859.

Typhus fever, scurvy, and rheumatism sometimes complicate the evolution of dysentery, being associated with this disease in the same patient. When the associated diseases maintain in their commencement, course, and termination an absolute independence, when they do not modify each other, the diagnosis is easy, and is to be made with due attention to the nosographic characters peculiar to each of them. When, however, the associated diseases modify each other, exaggerating or neutralizing some of their clinical manifestations, the morbid condition that results is of difficult appreciation at first sight. The diagnosis then becomes far from easy, and in order to form a sure and exact opinion, the practitioner must attend to the epidemiology of the locality, to the antecedents of the patient, to the manner in which the disease began, and to its evolution, carefully analyzing all the symptoms.

Prognosis.

The prognosis of dysentery varies extraordinarily according to the cases, according to the symptoms presented, according to individual conditions, the endemic or epidemic conditions, etc. Considered in the absolute and without reference to the ulterior influence of treatment, dysentery is a grave disease; even in its mildest forms,

those in which recovery is spontaneous or under the influence of inert means, the prognosis should always be reserved, not only because of ulterior complications and consequences of the disease, but also because it is not infrequent that a mild dysentery, acute or chronic, assumes from one moment to another extreme gravity by reason of the modifications and extension of the local process. As Delioux de Savignac correctly says, dysentery is a treacherous and insidious disease which, often causing no anxiety during the first days, and seeming to yield readily to treatment, is liable suddenly to exhibit extraordinary malignity and give rise to disorders which can be removed only with the greatest difficulty. In the tropics it is not uncommon to see a mild chronic dysentery, allowing the patient to attend to his usual occupations, interrupted in its course by a grave complication or by an acute attack, during which abundant hemorrhage from the intestines may be observed.

Cases of sporadic dysentery and that which develops in regional epidemics in cold and temperate climates, usually terminate in recovery; in them grave complications such as gangrene, suppurative hepatitis, hemorrhages, and peritonitis are rare. In the endemic dysentery of hot climates, besides these complications to which the patient is always exposed, the passage to the chronic state is to be feared.

In general, in persons depressed by hardships and privations, or weakened and exhausted by former diseases, and in those who have made forced marches or labored beyond their strength, dysentery assumes its gravest forms. One of the causes that concur most to increase the mortality of dysentery is the agglomeration of individuals and the pollution of the soil and air which results from it. The epidemics of armies on the march, and of the inmates of emigrant ships, prisons, and hospitals are always characterized by a high mortality.

Treatment.

The treatment of dysentery has always been influenced by the reigning nosological doctrines. It would be tiresome to enumerate all the methods of treatment recommended at different times for this disease, all of them based more or less on theoretical and preconceived ideas, and many of them having enjoyed great favor. It is true that all these processes of treatment effected numerous cures; favorable statistics were presented setting forth their advantages, which did not prevent their being abandoned later, when the pathological doctrines changed. To-day, being better acquainted with the natural evolution of dysentery and observing the facts with unbiassed

mind, we are able more accurately to estimate the effects of the older methods of treatment, and to lament the lives sacrificed to doctrinal exaggerations. Who at the present day can fail to be astonished at the organic resistance of the poor sufferers who had the good fortune to survive, in spite of the repeated bloodletting used to combat the intestinal inflammation?

Incontestably, modern practice possesses much more innocent and valuable resources for the treatment of dysentery; and if we have not yet a remedy worthy to be called a specific, we are at least able to limit the dissemination of the disease and sensibly diminish its mortality. Dysentery is to-day not only much less frequent but much less grave than formerly. The statistics of morbidity of dysentery and of deaths by this disease are decreasing everywhere. And this effect is undoubtedly brought about by the resources of modern prophylaxis and therapeutics.

Acute Dysentery.

Abandoned to its natural evolution, without the modifying influence of drugs, dysentery may terminate in recovery; in the majority of cases, however, if not properly treated, it will terminate fatally, or at least will be greatly prolonged, weakening the patient and exposing him to contract other diseases or to suffer the effects of a complication or a consequence of the dysentery. Especially in the tropics it is extremely dangerous to abandon the disease to itself, because in the great majority of cases it will terminate fatally or pass into the chronic state.

One of the principal conditions of success in the treatment of dysentery consists in beginning it as soon as possible. As a rule, every case of dysentery treated properly from the start will end in recovery. On the other hand, the longer the patient remains without treatment, the more rebellious will the disease prove to be and the greater resistance will it offer to the remedies.

Of all the drugs recommended in the treatment of dysentery, that which has given the best and surest result is undoubtedly ipecacuanha. It may be prescribed according to the Brazilian method: Take 4 gm. (ʒ i.) of ipecacuanha in powder, and 200 gm. (℥ vi.) of boiling water and let it steep for twelve hours; at the end of this time pour off the liquid to be administered to the patient, and keep the powder, pouring 200 gm. more of boiling water on it and leaving to steep for twelve hours, after which pour off the liquid as before to be administered to the patient; from the same powder make a third infusion in the same manner. The liquid resulting from each infusion and maceration is

administered in the course of a day, either all at once or in broken doses. On the first day the patient is sure to have nausea and repeated vomiting; on the second day there is usually nausea without vomiting, and on the third day the tolerance is almost always complete. Some physicians give a fourth infusion made with the same powder as the former ones; but it is so weak as to appear totally inert, and it is better to recommence the treatment on the fourth day with a little smaller dose (2 or 3 gm.) of ipecacuanha, which will serve for three successive macerations of twelve hours each.

Contrary to many physicians, I consider the vomiting and nausea provoked by ipecacuanha prejudicial to the patient, as it tends to debilitate him, to give him a repugnance for the medicine, and to suppress his appetite. Ipecacuanha, given according to the Brazilian method, is open to the objection that it always provokes vomiting and nausea, and many patients refuse to continue the treatment. I avoid these objectionable features by adding to the liquid resulting from each maceration some cinnamon and a small quantity of morphine and prescribing the mixture in broken doses, a wineglassful every two hours. Besides this, on the first day, fifteen minutes before each dose of ipecacuanha, I have the patient take twelve drops of the following mixture: Menthol 20 cgm. (gr. iii.), Jamaica rum 20 gm. (ʒ v.), tincture of opium 10 cgm. (gr. iss.); and order a mustard plaster over the pit of the stomach. Some physicians prefer the simple infusion of ipecacuanha with the addition of laudanum; others use the ipecacuanha in powder associated with calomel and opium. I have frequently used the following formula: Ipecacuanha in powder 10 cgm. (gr. iss.), powdered opium 2 cgm. (gr. $\frac{1}{3}$), calomel 5 cgm. (gr. $\frac{3}{4}$), in a capsule, one to be taken every two hours. In mild cases three grains of Dover's powders may be given with advantage, every two hours, either alone or associated with bismuth or salol, four or five doses being administered during the day.

Saline purgatives, principally the sulphates of sodium and magnesium, give very good results in the treatment of dysentery; their employment should always be advised when the ipecacuanha is not tolerated or does not prove efficacious, and it is sometimes proper to alternate the use of the salines and ipecacuanha. Saline purges should be prescribed in small doses, which may be repeated for two or three successive days; I commonly make use of the following formula: Filtered water 100 gm. (℥ iii.), sulphate of sodium 20 gm. (ʒ v.), or sulphate of magnesium 15 gm. [ʒ iv.]), gooseberry syrup 30 gm. (℥ i.). The patient is to take this mixture in two doses, with an interval of three or four hours between them. Saline purges are chiefly indi-

cated when there is constipation or when the evacuations are in small quantity and accompanied with violent tenesmus and colic. In mild cases or those of medium intensity, as well in acute as in chronic dysentery, I have obtained excellent results with the following treatment: On the first day I prescribe sulphate of sodium or magnesium, as above; on the second, third, and fourth days I prescribe the following formula: English magnesia 25 cgm. (gr. iv.), subnitrate of bismuth 40 cgm. (gr. vi.), ipecacuanha in powder 5 cgm. (gr. i.), powdered opium 2 cgm. (gr. $\frac{1}{3}$); in a capsule for one dose; the patient to take four doses a day, at intervals of three hours.

Opium, bismuth, and salol are valuable resources in the treatment of dysentery; they must be handled, however, with the greatest caution, because they are open to the serious objection that they produce constipation, and the rapid suppression of the diarrhœal flux in this disease is highly prejudical. The use of these remedies must, therefore, always be alternated with that of purgatives.

Besides the remedies I have already mentioned—ipecacuanha, saline purgatives, calomel, opium, salol, and bismuth—the indications of which vary in different cases, and even in the same patient according to the symptoms complained of and the course of the disease, recourse should be had to other auxiliary measures, which are always productive of good results, concurring to relieve the suffering of the patient and hasten his recovery. Such are small hot baths, hot poultices on the abdomen, or the application of a flannel soaked in hot water and covered with guttapercha, small emollient mucilaginous or albuminous clysters, and suppositories with opium, cocaine, or belladonna. When there are ulcerations in the rectum and sigmoid flexure, accompanied with great irritation and spasm, clysters of opium associated with bismuth may be employed with very good results.

Losch found that a solution of quinine of 1:5,000 killed the amœbæ. Councilman and Lafleur recommended the use of rectal injections of a watery solution of sulphate of quinine of 1:5,000 or 1:2,500. Harris says that he used this treatment with great persistence in some of his earlier cases, but in not a single instance was there the slightest perceptible result. In one case I used with excellent result quinine clysters of 1:2,000; I employed the following formula: Infusion of ipecacuanha 1 litre (O ii.), sulphate of quinine 50 cgm. (gr. viiss.); for three enemata. The rectal injection of a litre of solution is always borne with difficulty; I prefer to employ injections of 300 gm. (℥ x.) at most.

Permanganate of potassium has likewise been employed in clysters with good result. Trousseau advised the use of enemata of sulphate of zinc or sulphate of copper, and Delioux de Savignac speaks

highly of clysters of nitrate of silver followed by albumen and chloride of sodium. This last author also recommends rectal injections of iodine in chronic dysentery. I have employed these several means very seldom, and always in grave cases, which renders it impossible to form an exact opinion concerning them.

Chronic Dysentery.

Chronic dysentery is commonly more rebellious to treatment and more capricious than the acute. The methods to be employed are more or less the same—ipecacuanha, saline purges, calomel, opium, bismuth, salol, etc.; to these remedies may be added benzonapthol associated with salicylate or benzoate of bismuth and Dover's powders. The removal of the patient outside of the endemic centre is very beneficial and must be effected whenever possible. Besides this, recourse should be had to auxiliary means to combat the anæmia and other complications which may arise. Harris recommends the use of hydrogen dioxide; the ordinary commercial hydrogen dioxide is diluted from four to eight times with water, and the solution is injected. About a quart is injected twice daily, which, after a week, may be gradually decreased. This is the only agent, writes Harris, which has in his hands proved of any decided value.

Diet.—Much attention must be given to the diet of the patient, which, when well regulated, facilitates recovery. It is not infrequent that the appetite is retained in dysentery, the stomach and small intestine performing their functions normally; when this is the case, there is no reason to deprive the patient of food. Food of easy digestion and leaving little residue should be recommended; milk, eggs, and in general, albuminous and proteid substances are proper in these cases. In the more severe forms of dysentery or during acute exacerbations, accompanied with frequent calls to stool and violent colic and tenesmus, solid food should be suppressed and milk and skimmed broths prescribed. When milk is not easily tolerated, egg albumen may be recommended. When the period of aggravation has passed, feeding is to be resumed with great caution, at first only allowing semisolid foods of the consistence of cream, and strong and concentrated broths; then toasted bread, fowl, etc., the patient being always advised to take but a small quantity at a time.

Prophylaxis.

The prophylaxis of dysentery is dependent on its etiology and constitutes a subject worthy of the attention of physicians and public authorities. It admits of hygienic measures more or less identical with those employed against infectious diseases. During an epidemic of dysentery the patients should be isolated in their own dwelling or sent to hospitals and special infirmaries; every hygienic precaution should be taken to avoid the dissemination of the disease. The stools should be submitted to the action of disinfectants before being poured into cesspools or passed into the sewer. The cesspools should be constantly disinfected. It is proper always to have in the vessel which receives the dejections a certain quantity of an antiseptic solution (corrosive sublimate, sulphate of copper, or sulphate of quinine). All the clothing should be wrung out of boiling water. The room occupied by the patient should be disinfected according to the rules ordinarily followed. Much attention should be paid to the drinking-water; during epidemics, and whenever we cannot be certain of the purity of the water, it is proper to recommend the use of boiled water.

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YAWS.

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YAWS.

Definition.—Granuloma tropicum or yaws is a specific contagious, non-infectious disease, confined to tropical countries and communicated by actual contact of the virus with a breach of the surface of the skin. It is characterized by an incubation period of from ten days to six weeks, followed by an elevation of temperature—which may be slight or may run into continued fever—by rheumatic-like pains in the long bones of the limbs, and by an eruption of squamous patches which develop through a papular stage into distinctive yellow encrusted granulation tumors, which usually terminate in resolution without leaving any scars to indicate their sites. Micrococci are invariably found in the diseased tissues, and they are believed to be the specific microbes of the disease. The fully formed eruption has a loathsome appearance, and it exhales an evil odor. The disease attacks persons of all races exposed to its contagion, it is rarely fatal, it is not hereditary, it is chronic in its course, it does not greatly undermine the general health, it may terminate in spontaneous cure, and it is liable to relapse. One attack usually produces immunity from a second one, but the immunity tends to disappear in process of time.

Synonyms.

Yaws is the name that has been applied to the disease by the English from the time of the earliest introduction of African slaves to the American colonies. Originally it was the plural of yaw, which is even now employed to distinguish one of the characteristic neoplasms of the malady; but the plural form is now used as a singular noun to indicate the disease as a whole.

It has been erroneously asserted that the word yaws is of African origin, and that yaw is the term used in Guinea to designate the fruit of the raspberry. Unfortunately, however, for the theory, there are no raspberries in West Africa, and a careful official inquiry, made some years ago at the instance of the Colonial Office in London, established the fact that the names yaws and pian are not of West African origin. The term yaws is derived from the Celtic word *ias*, pronounced yas, which means heat, boiling or bubbling up, and is

the source of the English word yaw—the primary meaning of which is, according to Webster, "to rise in blisters, breaking into white froth, as cane juice in the sugar works." In view of this meaning the appropriateness of the name yaws, that was applied colloquially to the disease by those engaged in the slave trade, is evident.

The French term the disease *pian*, which is a pure Celtic word meaning a malady. *Epian* and *L'Epian* were terms used synonymously with la vérole and mal de Naples by the French in the seventeenth and the early part of the eighteenth centuries to distinguish syphilis, and at times pian was also used in the same way; but, in those days even as now, yaws and syphilis were often confounded with each other, although it is worthy of note that Lavoisier early last century emphatically asserted that "la vérole et les yaws sont deux maladies très-distinctes."

The Spaniards and the Portuguese and their descendants in tropical South America called yaws *bubas*, which, like pian of the French, was synonymous with syphilis—or lues gallica, as that disease was termed by the Spanish-speaking races. Indeed, in 1648, Piso alluded to bubas being mistaken for the lues gallica in Brazil.

The name *yaya*, according to Raymond Breton, who wrote in 1665, was used by the Caribs inhabiting the Antilles to denote yaws, and the name is still so employed by the Caribs of Dominica. According to old authors *pyans* was the term applied to syphilis by the Caribs.

The natives of West Africa, which appears to be the endemic focus of yaws, use a variety of names to indicate the disease; and, as will be seen from the following table of synonyms drawn up by Dr. Easmon, the chief medical officer of the Gold Coast Colony, there is no common root running through the names, and there is nothing whatever to connect them with yaws, pian, or bubas.

Sierra Leone, Lagos,	*Ogōdō.*
Fanti,	*Dūbé.*
Accra,	*Ajortor.*
Hausa,	*Tonjārā.*
Moshi,	*Toomah.*
Kroo,	*Soombah* (Grand Cess)
Kroo,	*Subanini* (Sinoe).
Soosoo (Sierra Leone),	*Dorgotch.*
Grushi,	*Sankorr.*
Crepi, Kitta,	*Jahtor.*

In the Fiji Islands, in Polynesia, the disease is known as *coko* (pronounced thoko) and in New Caledonia it is called *tonga*.

There is nearly as great a diversity in the scientific terminology of the disease as in the colloquial names. Most of the older writers,

failing to differentiate it from syphilis, called it *lues venerea*, and Sydenham wrote of it as the venereal disease, and suggested that it should be named *syphilis æthiopica*.

Sauvages, in 1761, coined the term *frambœsia* from the French word framboise, as he considered that the granulomata when divested of their crusts resembled raspberries (a resemblance the author thinks a far-fetched one) and he made two varieties of the disease, viz., *frambœsia Americana* and *frambœsia Africana*. Frambœsia is now often used by modern writers, but it would be much better to discard it altogether.

Swédiaur, in 1798, believing that the disease bore some analogy to the thymus of ancient authorities, termed the malady *thymiosis*.

Mason Good, in 1825, discarded frambœsia which had been employed by Cullen in his "Nosology" and called the disease *anthracia rubula*, but he said that *morula*, from morus—a mulberry, would be a more appropriate designation, and that name has been adopted by the London College of Physicians in their official "Nomenclature of Diseases" as the Latin equivalent of yaws.

Alibert, in 1832, considered yaws to be a variety of mycosis, and he applied the term *mycosis frambœsioides* to it, including under the name *mycosis syphiloides* a number of endemic varieties of syphilis.

In 1881, Charlouis described yaws under the name *polypapilloma tropicum*, considering doubtless that the granulomata were of a warty nature. Hamilton, in his work on "Pathology," points out that the type of structure of the papillomata is based on that of a papilla, the distinction being only one of degree. In a papilloma the blood-vessels are enlarged and dilated, the connective tissue is much increased in quantity and forms the bulk of the growth, and the epidermal covering is greatly proliferated; whereas the enlarged papillæ of the yaws granulomata are made up chiefly of granulation cells and the papillæ themselves are devoid of all epidermal tissue, the external protection being afforded—as will be seen later on—by the yaws crusts. The term polypapilloma, therefore, as applied to the disease is misleading, for it gives a mistaken idea of the minute anatomy of the characteristic tumors.

In the report of the West Indian Yaws Commission, published in 1893, the author objected to morula and frambœsia as the scientific designations of yaws, and he suggested the term *granuloma tropicum* in the following words:

"The word morula, however, is no improvement on frambœsia, for only in exceptional instances can the local manifestations of the disease be considered to have a slight resemblance to a raspberry or mulberry. If nomenclature is to depend on analogy, the analogue

should bear correspondence to some common characteristic, and not to exceptional appearances that may often escape observation. A more scientific way of naming the disease would be to apply to it a term expressive of one or more of its attributes, and to that end I may perhaps be permitted to suggest that *granuloma tropicum* be accepted as the Latin equivalent of yaws, for the granulomata are characteristic of the malady which prevails only in the tropics."

History.

Several of the earliest writers on yaws thought the disease to be identical with Tsara'ath, the leprosy of the Jews, as described in the thirteenth chapter of Leviticus; and Adams in 1807, and Bateman in 1817, held to the same opinion. The author has dealt at some length with this question elsewhere, but it may be stated here that the scriptural accounts of the several diseases included under the name that has been translated into the word leprosy are altogether too vague to enable them to be identified at the present day, and there is nothing whatever in the symptoms described to justify the assertion that Tsara'ath was yaws.

Ali Abbas, an Arabian physician of the tenth century, described leprosy in his "Theoria" (cap. 16, lib. 8) and closely followed the Mosaic account of the Jewish disease; and this has been deemed sufficient by recent writers to authorize the statement that yaws was described by him, but the symptoms detailed in the "Theoria" do not correspond with those of yaws, and therefore it is incorrect to cite Ali Abbas as the earliest writer on the disease.

Yaws undoubtedly existed in West Africa from the earliest time of which there is any record. At the commencement of the slave trade it was found to be endemic in the countries bordering on the Gulf of Guinea, and writers bear evidence to the fact that slaves were landed in tropical America with the yaws upon them.

The mistaken belief, held by so many of the earlier writers and continued down to the present day, that yaws is identical with syphilis, has caused the history of the two diseases to be brought into a state of confusion. The opinion was enunciated by many medical men of the seventeenth and eighteenth centuries that syphilis, which broke out with such virulence in the armies in Italy in 1493–94 and spread rapidly through Europe, had been brought from the Antilles by the soldiers of Columbus on their return from the first voyage of discovery. And, as the names then given to syphilis were afterwards applied to yaws, it was held by many that yaws in the Antilles was the parent of the syphilis that raged in Europe.

The fleet of Gonsalvo, however, which conveyed the Spanish soldiers to Italy, arrived at Messina in 1495, that is two years after syphilis was spreading at Naples in the army of Charles VIII. of France.

Gruner ("De Morbo Gallico Scriptores Medici et Historici," Jena, 1793) and others assert that syphilis was not carried to Europe from the New World, but that it had taken on an epidemic form among the Moors and Jews, who were expelled from Spain under circumstances of great distress and cruelty from 1487 to 1492. It is clear, then, from this and other evidence that syphilis originated in the Old World, and that it, like yaws, was carried to America. After its introduction it spread rapidly in tropical America; and Oviedo, in 1535 ("La General y Natural Historia de Las Indias," Sevilla) found it prevalent in Santo Domingo. Oviedo's account of syphilis has been mistaken for that of yaws, and he has been erroneously cited by writers as the first author who treated of the latter disease. The earliest writer, however, who gave a fairly accurate account of yaws, and at the same time distinguished it from syphilis, was Piso ("De Medicina Bræsilium," Lugduni Batavorum, 1643). He said the disease was introduced into Brazil by the African slaves, that it was called bubas by the Spaniards and Brazilians, and that it was mistaken for the lues gallica. Hillary in the West Indies, in 1759, and Winterbottom in Africa, in 1770, were the first authors to describe the disease under the name of yaws.

There is no evidence to establish the fact that yaws was endemic in tropical America during the first century and a half after its discovery; and the practical immunity of the Caribs of the present day from the disease, owing to their extreme cleanliness, tends to show that it was not prevalent among these aborigines. The remnants of the race in Dominica and St. Vincent are free of yaws which occurs commonly among the negro population of the lands contiguous to the districts reserved to the Caribs. Raymond Breton and de Rochfort, who wrote in 1665, and du Tertre, whose work on the Antilles was published two years later, speak of "pyans" and "epian"—the early forms of pian—as prevailing among the aborigines. But the hereditary nature of the disease and other diagnostic characteristics clearly prove that it was syphilis; indeed, du Tertre states that epian is "la veritable vérole dans le plus haut degré de sa malignité." It is clear, therefore, that those authors who have quoted the works of these old missionary priests as authority for the theory that yaws was endemic in the West Indian islands when they were first discovered, have not taken sufficient care to eliminate error by studying carefully the original works themselves.

Piso, as has been shown, bears evidence to the fact that the yaws was introduced into South America by the African slaves. Hillary says it "was first brought from Africa by the negroes into America and its islands," and there is a consensus of opinion to that effect among the writers of his day and those of the early part of the nineteenth century. The author, in the report of the West Indian Yaws Commission, discussed the matter at some length and arrived at the conclusion that yaws was found in America only after the initiation of the slave trade, and that it was introduced into the Western tropics by the negroes from the coast of Guinea. The history of the disease in the West Indies subsequent to its introduction was fully investigated by the Yaws Commission, and it is given in detail in the report. Briefly it may be stated that the planters—who were well aware of the contagiousness of the malady—segregated the affected slaves in "yaws-houses," which were erected in isolated positions and placed under the care of old negresses who had had experience in the treatment of the disease. The medical men who attended the slaves on the estates were not expected to interfere with the treatment of "the negroes in the yaws," and the dread which prevailed at that period of the contagion of so loathsome a disease caused them willingly to fall in with this arrangement. Subsequently, however, some of the abler practitioners in the colonies made a careful study of yaws; and the writings of such men as Hume, Hillary, Wright, Moseley, etc., brought to light many interesting facts concerning the disease and its treatment, and helped greatly to establish the non-identity of yaws and syphilis. After the slaves were emancipated the careful and successful efforts made by the planters to prevent the spread of yaws necessarily came to an end, but the disease was not often observed, as the negroes were left to themselves and the number of medical practitioners in the islands became greatly diminished. Many of the negroes, too, squatted on inaccessible crown lands and abandoned estates far away from the centres of civilization, and their hygienic conditions were as bad as it was possible for them to be. The few cases of yaws that had been turned loose from the old "yaws-houses" acted as *foci* for the dissemination of the disease, and the constant association of infected with healthy persons bred a contempt among the people for the manifestations and consequences of the malady. The result was that the disease spread rapidly in some of the islands; and, after a time, serious yaws "questions" sprang up in the colonies, so that the governments were forced to adopt measures for its repression. In Dominica, Grenada, St. Lucia, and other places it prevailed epidemically, and special yaws hospitals were established to segregate the worst cases. In the report of the West Indian Yaws

Commission it is shown that during the seventeen years ending 1891 over eight thousand yaws patients were treated in these hospitals at a cost of £35,000, and that a great number were also treated as dispensary patients by the district medical officers. At the present time there are yaws hospitals in Dominica, St. Lucia, Grenada, and Nevis, and there is also special legislation concerning the treatment of cases by the district medical officers in Trinidad and Tobago. The malady is prevalent in the other West Indian islands and in British Guiana, but the governments are precluded from adopting repressive measures, mainly on account of financial considerations.

Prout inclines to the belief that "West Africa was the home of the disease, and its spread over the world was due to the exportation of negro slaves." It may now be considered as an established fact that yaws was so carried to tropical America, and it was probably carried also by slaves to various parts of the old-world tropics; but there can exist no doubt now that there was an endemic *focus* of the disease in certain tropical islands of the Pacific Ocean. It was said a considerable time ago that the coko disease of the Fiji Islands and other parts of Oceania was identical with yaws, but the descriptions given of coko were not such as to establish this identity to the satisfaction of the author, who wrote as follows on the subject in the report of the Yaws Commission: "Although there exist in Oceania certain diseases bearing a resemblance to yaws, their identity with it has not been established in so conclusive a manner as to place the question beyond the region of doubt." D. C. W. Daniels, of the British Guiana Medical Service and formerly of the Fiji Medical Service, has brought forward evidence to show that yaws and coko are undoubtedly the same disease. Coko has existed in the Fiji and other islands of the Pacific from the time of which there is any record. The natives state that it has always been present, and they hold to the belief that it is better for the children to pass through an attack, as the disease is of greater severity in adult life; and, to that end, unaffected children are made to sleep with infected ones, and if that fail inoculation is practised.

As will appear when the questions of geographical distribution and diagnosis come to be treated of, diseases occurring in Ceylon, the Moluccas, and parts of India have been thought to be identical with yaws. A careful consideration of the symptoms detailed as present in these diseases leads the author to the conclusion that they are not yaws, and therefore he has not entered into any account of their history here. It may be that, later on, when accidental complications are eliminated and more attention is given to essential points

in diagnosis, it will be found that yaws has other endemic *foci* than those set down in this article. Meanwhile, in an exact account of the disease, doubtful examples of it must necessarily be excluded.

Geographical Distribution.

Yaws is now endemic in certain portions of the old and new world tropics; but, owing to the fact that it has been confounded with a number of ulcerative diseases, there is extreme difficulty in mapping out its exact geographical distribution. The descriptions of yaws in some of the text-books are not sufficiently accurate to enable one having no experience of the disease to diagnose every case with certainty, and to this is due doubtless the mistaken identity with yaws of syphilis, tubercle of the skin, and other ulcerative maladies. As will be seen later on, uncomplicated yaws is essentially a non-ulcerative disease, and to the fact that this characteristic has not been sufficiently insisted on by authorities is to be ascribed the confusion that has existed as to its attributes, and therefore its diagnosis and geographical distribution.

The disease prevails to a greater or less extent throughout the tropics of the new world. It is found in various parts of Central America, and in Venezuela, the Guianas, Brazil, and other tropical portions of South America. In the West Indies it is especially prevalent; and, in fact, it is now endemic in those tropical parts of America whither most of the African slaves were carried. In several of the British West Indian islands, as has been seen, the disease has at times taken on an epidemic form, and it has been found necessary in them to adopt special legislation and to establish yaws hospitals to cope with its ravages. At the present time yaws is found in all the principal West Indian islands extending from Jamaica to Tobago, with the exception of Barbados where cases are rarely seen.

It is said to prevail in all parts of tropical Africa, but the west coast has always been its endemic focus. It is also found in Mozambique and the neighboring countries, and Madagascar and other islands lying to the east of the Continent are infected, while cases are occasionally reported in North Africa, in the Soudan, and along the caravan routes in Central Africa.

The evidence as to the existence of the malady in Asiatic countries is not conclusive to the author's mind. A consideration of Sir William Kynsey's exhaustive report on the Parangi disease of Ceylon will show that several diseases are included under that term, and much evidence is wanting to establish the identity of yaws with any

one of them. Parangi is a Singalese name meaning foreign, and it was applied in the first instance to syphilis which was introduced into Ceylon by the Portuguese or the "foreigners" as they were called. It is an undoubted fact that several of the forms of disease now classed under the name Parangi are of syphilitic origin; and it would be more accurate to give the name as a synonym of syphilis instead of yaws as some writers do now.

A very large number of natives of India have been brought to the West Indies owing to the dearth of reliable agricultural labor consequent on the abolition of slavery, but there is no recorded instance of anything like yaws having appeared in these immigrants prior to their association with persons affected with the disease on the West Indian plantations. When, however, they have mixed with the negro inhabitants of the islands they have suffered greatly by the spread of the malady among them. Indeed in some of the West Indian yaws hospitals the East Indian coolies have at times formed the bulk of the inmates; and in St. Lucia, according to the report of the Protector of Immigrants, every care was taken to prevent the disease being introduced into India by the returning coolies; he states that "the most scrutinizing examination by experts was made of every man, woman, and child before embarkation."

In Assam and the Malay states yaws is said to be met with, but the author has not seen any description of the disease sufficiently detailed to determine its exact character with certainty. Nor does it appear that those who have made the diagnosis have had any experience of undoubted cases of yaws as they are seen in Africa and the West Indies.

The ulcerative disease known as pateh and bouton d'Amboine, which occurs in the Moluccas and spreads among the Malay inhabitants, has different characteristics from yaws, and it appears to be identical with the so-called "oriental sores" found in the East and the southern and eastern Mediterranean regions.

Dr. Daniels has determined the point that the coko disease of Fiji is really yaws. It is authoritatively asserted that syphilis is unknown among the Fijian natives, and that yaws or coko is so prevalent that practically all the children are attacked, the usual age being two years, for the disease is extremely rare in earlier infancy. Yaws is also found in the Samoan and Loyalty groups, as well as in the Tonga, Society, and Navigator Islands, and doubtless none of the Polynesian islands is entirely free of the malady.

It would be a curious fact were it to be determined that yaws does not occur in Asiatic countries when it prevails in the tropics of America, Africa, and Oceania. As close attention is paid to the

diagnostic features of the disease, and cases of syphilis, scrofula, etc., are carefully eliminated, it will doubtless be found that yaws does occur in parts of Asia, for all the conditions are present for the spread of the malady, and it has been found by West Indian experience that Asiatics are peculiarly susceptible to infection.

Etiology.

Contagion.—Yaws is a contagious disease, the virus finding an entry into the system through some break in the skin and not operating through the atmosphere. It is easily inoculable, as the author has proved by actual experiment; and the older writers on yaws in the West Indies speak of the practice of the negroes during the time of slavery inoculating their children so that immunity in after life might be established. In most instances the disease is spread by the direct contact of the healthy with the sick. But the contagion may be carried by flies, and it moreover clings to huts in which yawsy negroes have lived in poverty and squalor. In tropical countries flies are an ever-present intolerable nuisance at certain seasons of the year, and unprotected sores and skin eruptions attract these pests in great numbers. In the West Indies several species of *sarcophagæ* are known as "yaws flies," and reliable evidence has been collected of simple sores being infected with the virus of the disease by means of these flies. The contagium is undoubtedly a microbe; and, as will be seen later on, there is reason to believe that this is a micrococcus—having under culture definite characteristics—which is invariably found in the diseased structures. Pure cultivations of it have been obtained from the dust swept off the floor of a yaws hospital and kept in a dry place for several months. The contagion varies considerably in intensity; for while at times it is so virulent as to cause the disease to prevail epidemically, at other times healthy persons may associate with those suffering from yaws without risk, provided proper precautions be observed. Cases are on record in which nurses in charge of yaws wards have contracted the disease, but these cases are very few, although the nurses handle the patients with an indifference to risk that is bred of long familiarity. The author's experience shows that certain persons are ordinarily immune without having undergone an attack of the disease, and it would appear that most of the attendants at yaws hospitals are included in this category.

Race.—The erroneous opinion that the dark-skinned races alone are attacked was formed by the earlier writers who saw the disease only among negro slaves in the rigidly isolated "yaws-houses" in which all cases of the disease were segregated. This opinion has

been widely copied by subsequent writers. The fact, however, is that there is no racial immunity. The prevalence of the disease among the poorer people in those countries in which it is endemic is due to their overcrowding in dirty hovels and to other hygienic defects favoring the operation of the contagion. Europeans and Asiatics living under the same condition as the negroes in the West Indies, as is often the case, are as liable to contract the disease as are the negroes themselves. And cases are on record in which persons of all races in the upper ranks of society in endemic centres have been attacked with yaws in consequence of careless contact with people afflicted with the disease. As yaws is a malady confined to the tropics, and as the vast majority of the inhabitants thereof belong to the dark-skinned races, it necessarily follows that it mainly occurs among the poorer people of the laboring population, for such are its attributes that poverty, squalor, and defective sanitation generally favor greatly its propagation.

Climate.—Yaws, as has already been pointed out, is essentially a disease of the tropics; and there is not, so far as the author knows, any authentic case recorded as having been observed in temperate climates. This characteristic at once establishes a line of demarcation between yaws and the closely allied maladies, viz., tubercle, syphilis, and leprosy, of which Sansom, in one of his Milroy lectures, in 1890, truly says: "They produce growths that are strikingly similar in pathological character, and they either are or have been universal in their distribution apart from consideration of climate, race, and habits of life."

The disease is invariably more prevalent shortly after wet weather sets in, and this is due as much to more vigorous growth of the specific microbes in a moist atmosphere as to the longer periods spent by the people in such weather inside infected huts whereby they are subject for greater lengths of time to the operation of the contagion.

Diet.—Theories have been propounded that there is a connection between the diet of the people and the spread of the disease, and salt fish has been fixed on as the special food that is in some way concerned with the manifestation of yaws. The official inquiry conducted by the author established the fact, however, that in those West Indian colonies where yaws most prevails there is the least consumption by the people of salted food.

The laboring population of the tropics, and the poorer people residing therein, live mainly on vegetable food, so that large quantities of plantains, rice, etc., have to be ingested to provide the necessary quantity of nitrogenous matters for the repair and building up of the tissues of the body. The conclusion of the West Indian Yaws

Commission on this question of the relation of diet to yaws was as follows: "A careful consideration of all the facts can lead to no other conclusion than that the diet of the people of the West Indies, by giving rise to disorders of the digestive organs, affects the nutrition of the body in a deleterious manner, thereby not only predisposing the system to react to morbid influences but also modifying the course and termination of any disease that may become established. As regards yaws, however, it appears that diet has no influence whatever in its origination, or its spread among the populations of the various colonies."

Heredity.—Some of the earlier writers on yaws, owing to the disease being confounded with syphilis, declared it to be hereditary, but careful study of its attributes in recent years establishes the fact that it cannot be transmitted by the parent to the offspring. Dr. Tulloch, whose experience of yaws in Tobago is unique, states: "It is never hereditary," and this emphatic assertion is in accord with the author's experience. Indeed it may be mentioned that a number of births have taken place in the yaws hospitals in Dominica that have been under the author's direction; and, although all the mothers were affected with the disease, in no case did the children manifest any congenital or later hereditary symptoms of yaws. It is very rare indeed to see an infant attacked under two years of age, and when it does occur it is invariably found that a wound or sore has been infected with the virus.

Age.—No age exempts from the operation of the contagion, but the great majority of the cases occur in children between five and fifteen years of age. In the tropics young children of the laboring classes, even in civilized centres, are either scantily clothed or almost or entirely naked, and whilst they are playing together the disease is spread as the result of contagion by actual contact, for the negroes never dream of isolating cases of yaws. The following table, drawn up by the author from seven hundred and thirty-nine patients treated in a yaws hospital in Dominica, shows how far age may be considered as a predisposing cause of the disease:

Age.	Under 5 years.	5–10 years.	10–15 years.	15–20 years.	20–30 years.	Over 30 years.
Number of cases	120	236	142	65	78	98
Percentage	16.2	31.9	19.2	8.8	10.6	13.3

From these statistics it is seen that from five to ten years is the period of life during which the disease is most liable to occur, and that 67.3 per cent. of the cases occur before the age of puberty.

Sex.—An analysis of 3,115 cases admitted during the years 1880–90 to yaws hospitals in the West Indian colonies showed that 1,913 or 61.4 per cent. were males, and that 1,202 or 38.6 per cent. were females. In round numbers, therefore, it may be said that the disease attacks males and females in the ratio of three to two. This proportion, however, is modified according to age, for it is found that in adult life the cases of affected females exceeds that of the males. This is due to the fact that women by their indoor life and longer and closer contact with the diseased children are more liable to infection. The following interesting table compiled from 273 cases treated in one of the Dominican hospitals shows at a glance the liability to infection at various ages:

Age.	Total number of cases.	Males.	Females.	Percentage.	
				Males.	Females.
Under 5 years............	38	24	14	63.2	36.8
5–10 "	94	60	34	63.8	36.2
10–15 "	60	42	18	70.0	30.0
15–20 "	28	15	13	53.6	46.4
20–30 "	29	13	16	44.8	55.2
Over 30 "	24	10	14	41.7	58.3
Totals...............	273	164	109	60.1	39.9

Previous Disease.—The debility that exists during the convalescence from most general diseases renders the patients more susceptible to the contagion of yaws and other similar maladies. This, however, is simply due to the fact that there is less resistance to the impression made by any morbid poison in debilitated states of the constitution whether produced by disease, fatigue, fasting, or any other depressing cause; and it cannot be said that there is any disease an attack of which leaves a special predisposition to yaws. But the case is different in regard to those maladies and local injuries that cause a break in the continuity of the surface of the skin, and thus present sites for the easy entry of contagious matter. Cleanly persons with whole skins apparently associate with impunity with those suffering from yaws, but there is no such safety as regards persons with cutaneous lesions. Skin diseases due to uncleanliness, and to animal and vegetable parasites as well as to insect bites are common in the tropics, and the scratching of the irritated surfaces produces small sores that are liable to be infected with the yaws virus.

Symptomatology.

The *stage of incubation* extends ordinarily from ten to fifteen days; but in a small number of cases it will be lengthened to six weeks. It has been stated that the disease may incubate for a much longer period, even to six months, but such assertions have not been supported by any satisfactory evidence. In most cases there are no prodromic symptoms noticeable; but, shortly before the evolution of the eruption and for a variable duration afterwards, pains of a rheumatic character, sometimes very severe, may affect the long bones and joints, especially at nights, and in these instances anorexia and malaise are present.

Invasion.—The onset of the eruption may also show no deterioration of the general health, but it is frequently marked by an elevation of temperature which is generally so slight as to escape observation. In a small proportion of cases, however, there is considerable constitutional disturbance lasting for a few days or even a week or more. The fever is usually preceded by a rigor and it is of a continued type —the temperature ranging from 100° to 103° F. with nightly exacerbations, and there may be some diarrhœa present. The ordinary subjective and objective phenomena of the febrile condition are present, but there are no diagnostic characteristics except that the "yaws pains" persist and are usually accompanied by severe headache. When the fever is on the decline the typical eruption begins to evolve, and its onset and course are the same in the febrile as in the non-febrile cases.

There is no initial lesion, as has been erroneously asserted by a few writers, in either the inoculated or the acquired disease. The eruption may be scanty or general, but there is no one lesion which differs essentially from the others or is capable of being pointed to with any degree of reason as the initial one.

The *eruption* is of three forms which are now usually designated squamæ, papulæ, and granulomata. They are simply, however, three stages of one eruption, the squama developing into the papula which in time becomes the granuloma. But, by abortion, one stage may persist as a distinct eruption, or all three stages may be seen in the same individual at the same time from the commencement to the decline of the disease.

Squamæ.—The skin becomes harsh and dry, and whitish raised patches of furfuraceous desquamation appear at various parts of the body and limbs. These patches are very noticeable in the dark-skinned races (Fig. 12). They are usually small and round in contour, but

they may be of an irregular shape, or, more rarely, they may be disposed in rings enclosing unaffected skin. In a small proportion of cases the patches coalesce and involve large areas, or the whole skin may become affected and appear as though dusted with flour. In some instances the squamæ are not well marked, they are not elevated

FIG. 12.—Granulomata and Squamæ of Yaws.

above the skin and their character can only be detected by a lens, by which means the exfoliation of the horny epidermis can easily be made out, the flakes of epidermis being seen free at one end and attached at the other so as to give a ragged appearance to the affected portion of the skin. The squamæ are the first local manifestations of the disease, but they may persist throughout the attack or appear as a distinct eruption at any period of its progress. These squamous patches are called by the negroes in the West Indies "dartres" or "yaws cocca."

Papulæ.—After some days papules will be observed to have formed in certain of the squamæ. On examination with a lens magnifying not less than twenty diameters these papules will be seen to be pushed up from the rete Malpighii through the horny epidermis, which breaks over their summits and splits in lines radiating from the centre, the necrosed segments curling away from the increasing papule. When the papules become about a millimetre in height and breadth a yellow point may be observed on the summits, and this has been described by many writers as a drop of pus under the epidermis. But by means of a lens the yellow spot is seen to be a naked cheesy-looking substance which cannot easily be detached. Frequently a hair will be observed issuing from the yellow spot, thereby indicating that the hair follicle is the centre of the changes taking place. This papular stage is called by the negroes "gratelles" or "guinea corn yaws." It may persist during the entire period of the disease, or it may appear at any time during its progress. When a general eruption of papulæ reappears as a late symptom the case will be a protracted one.

Those papules that remain without further development become altered in form after a time. The summits are depressed, the concavities being lined with the yellowish cheesy material. Such papules persist often about the knees and elbows, but they may be met with at other parts of the limbs or on the body, those parts liable to exposure being most often affected.

Granulomata.—In normal types of the disease, the papule increases in size until what is known as the "tubercle," or "yaw," or "bouton pian" is formed, and this is the characteristic local manifestation that has occasioned the names frambœsia and morula to be given to the malady.

The various stages of evolution from the squama to the granuloma are best seen at an early period of the disease. A portion of a squama having developed into a papule, the papule increases in size in all directions; and, as it grows, the minute yellow mass at the summit widens so as to form a cap of yellow incrustation on the tumor. These tumors or granulomata are seen usually as round elevated growths from an eighth of an inch to several inches in diameter, or even larger, and their crusts are of different shades of yellow or brown. The smaller tumors are invariably rounded at their summits and edges, but the larger ones may be flat-topped, tuberculated, or depressed in the centre. The large tumors vary greatly in size and shape. The author has met with cases in which the whole cheek, or the whole popliteal space, or dorsum of the foot, has been occupied by confluent masses of encrusted granulomata; and in these in-

stances the surfaces of the crusts were irregular and sometimes fissured. Rarely, too, the crusts may be entirely or partially absent, and then a reddish or pinkish tuberculated mass is seen. The outline of such confluent masses is always irregular, being made up of various curves.

In isolated granulomata the circular form is most often seen; but at times they are ovoid or reniform, or they may be annular, enclos-

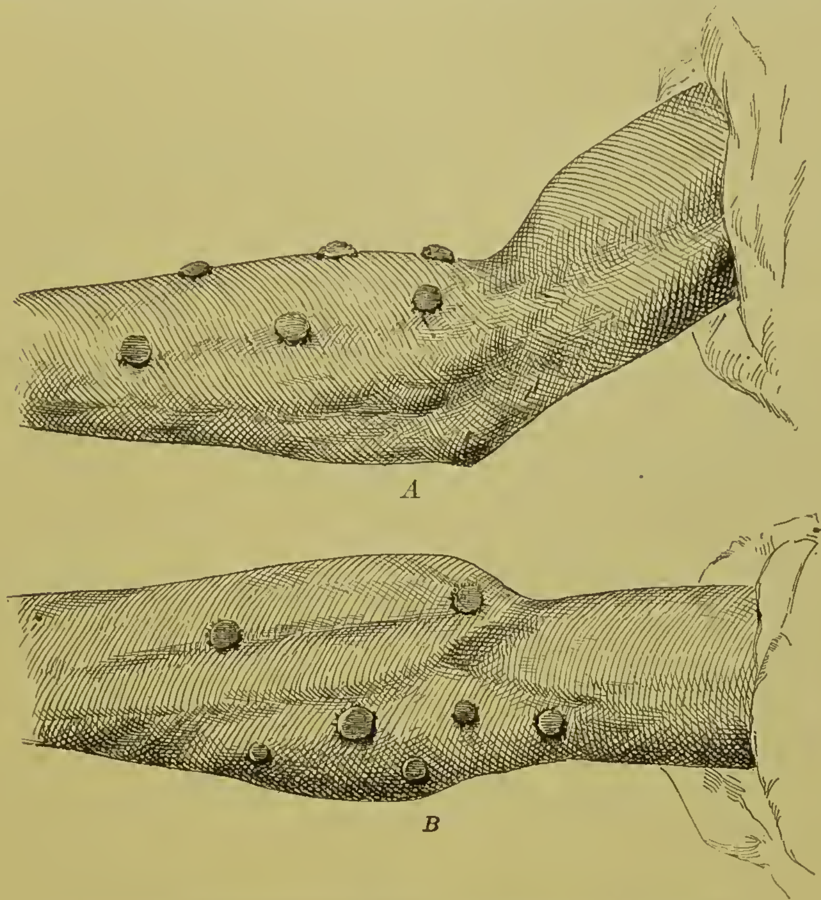

FIG. 13.—Granulomata on the Arm. *A*, Side view; *B*, front view.

ing sound skin. They are frequently observed about the nostrils, mouth, and anus, where they may implicate the mucous membrane; and in a few cases, as a result of autoinoculation, these orifices may become encircled by a coalescence of contiguous tumors. In such situations, more especially at the anus, the moisture, friction, and muscular movements cause the crusts to be softened and detached, and the granulomata are then either coated with a yellowish-gray viscid exudate, or they present the appearance of pale reddish or pinkish fungoid masses.

After a time the crusts lose their bright yellow color, they become in places stained with blood and marked with dark spots and lines

due to the accretion of dirt, epidermal scales, etc., and in appearance they are very like the soiled rind of cheese. When the granulomata disappear by absorption in the later stages of the disease, the crusts become thin, dry, and brownish or even black in color. The crusts are firmly adherent, and they usually break when forcibly torn off. When they are raised, there will be seen beneath them reddish fungoid tumors springing from the dermis. Here and there may be observed slight hemorrhages due to the forcible detachment of the protective coverings of the tumors. After their removal the crusts are soon reformed by the exudation of a pale yellowish-gray material which rapidly inspissates. There is ordinarily no secretion of pus, and the term "pustulo-tubercular" applied by writers to the eruption has been given in ignorance of the real character of the growth.

When the granulomata are subjected to constant moisture and friction, as when they are situated in the anal fissure, their non-encrusted surfaces become smooth, flattened and callous, and their color varies from yellowish-gray—like sodden chamois leather—to a pale pink. In rare instances large masses of non-encrusted granulomata are observed about the lower extremities, and they are called by the negroes the "master" or "mother" yaw, the popular fallacy being that they are the source of the disease. These masses may be formed by the coalescence of contiguous tumors, or by the infection of an innocent ulcer. In 1,182 cases of the disease examined by the author, only 26, or 2.2 per cent., were found to have the so-called mother yaw.

The granulomata hardly ever give rise to pain and they are not endowed with much sensibility. The crusts may often be torn off without the patient's experiencing even discomfort, and the application of escharotics is usually not a painful operation. In the West Indies it has long been the practice of the native yaws curers to determine the nature of doubtful eruptions by the application of the acid juice of the lime fruit to them. If this process prove painless, the disease is pronounced to be yaws.

In a well-developed case of the disease in a negro the yellow-capped tumors present a striking and loathsome appearance, and they exhale a peculiarly disgusting and characteristic odor; indeed, the author has often detected cases of yaws by the sense of smell alone.

When the granulomata attack the soles of the poorer people of the West Indies who walk with bare feet, the thick, hard, and leathery epidermis forms an obstacle to the outward growth of the tumor, and a condition is produced which is known locally as "tubboes," or "crabs," or "crappox." The pressure caused by the confinement of the increasing tumors between the thick unyielding epidermis and

the plantar fascia gives rise to much pain and tenderness, so that the patients are unable to walk without considerable suffering. After a variable time the epidermis becomes sodden and softened, and it gives way over the centre of the granuloma which then rapidly grows up until it reaches a quarter of an inch or more beyond the level of the surrounding skin, which becomes ragged and uneven, as if eaten away by the application of a corrosive liquid. Granulomata in the soles, for obvious reasons, are never encrusted: they are usually pale pink in color, and smooth on the external surface, on which may be

FIG. 14.—*A*, Dermatitis of the Soles of the Feet; *B*, Dermatitis and Granulomata of the Soles of the Feet.

seen at times a scanty, viscid, yellowish secretion. It has been asserted that "tubboes" are sequels of the disease, but this is an error, for they are met with at all the later stages of the disease. An examination of three hundred consecutive cases, admitted to one of the yaws hospitals in Dominica under the author's direction, showed that tubboes evolved with granulomata on other parts of the body in thirteen cases, and that in only eight cases did they appear as late symptoms, and even this delay was probably due to the obstacle presented by the hard epidermis of the sole. It must be noted that any circumscribed tumor pushing its way through the hard and thick epidermis of the sole of a person who walks barefooted will give rise to appearances identical with those of the yaws granulomata in such a situation.

So, if the tubboes be the only manifestation, care must be taken to avoid an error in diagnosis, as the case may not be one of yaws at all.

The terms "crabs" and "crappox" are also applied to a chronic dermatitis that at times affects the palms of the hands and the soles of the feet of the negroes in the West Indies, but in some of the islands it is usual to call this inflammatory condition "dry crabs" or "dry crappox" in order to distinguish it from the yaws granuloma. Such dermatitis may be seen infrequently accompanying yaws, and it is somewhat like an enlarged and otherwise exaggerated squamous patch, but the author has observed it in persons who have never been affected with the disease, and it is not uncommon in the island of Anguilla which is quite free of yaws and apparently has always been so. It is undoubtedly the outcome of irritation caused by dirt for the most part, and it occurs only amongst those engaged in agricultural pursuits. It usually affects the external portions of the skin, the upper layers of the epidermis being proliferated and eroded and at times splitting into laminæ which flake off entirely or separate partially, giving a very ragged appearance to the skin. In a few instances the inflammation extends deeper, the epidermis being fissured and exposing the rete Malpighii which then exudes a serous fluid; in such cases, naturally much pain and tenderness result.

The granulomata in mild cases of the disease may be solitary; or, in severe types, they may appear as a general eruption in successive crops involving the face, head, neck, body, and limbs. In fact, when the tumors are small, the eruption is not unlike an exanthem, and some of the older writers classed the disease with smallpox and other such maladies. The eruption is usually symmetrical, and it is oftenest seen on the anterior and exposed portions of the body. An examination of 100 consecutive hospital cases by the author showed that the fully-formed eruption appeared on the face and head in 49 cases, on the trunk in 20 cases, on the genitals in 16 cases, on the perineum in 20 cases, on the upper extremities in 29 cases, and on the lower extremities in 70 cases. In 3 cases only was the scalp affected, and in no case were the tumors found in the axilla. In nearly all the instances in which the perineum and genitals were affected the cases were those of children.

Ordinarily the tumors are found only on the true skin, but in rare instances they are seen on the mucous membranes of the nose, lips, and mouth, and rarer still they are met with on the glans penis and the prepuce. An examination of 750 patients admitted to one of the Dominica yaws hospitals showed that the mucous membranes were implicated in only 21 or 2.8 per cent. of the cases. In nearly every

instance, however, the implication of the mucous membranes is due to an extension of the granulomata from contiguous skin. In over five thousand cases of the disease examined by the author he met with only ten examples of isolated granulomata on the mucous membranes, the mouth and the nostril being the site selected.

The granulomata increase in size and attain their maximum growth usually within two weeks of the time of their evolution from the papule. In favorable cases they remain stationary for several weeks, and then commence to disappear by absorption in the following manner: The crusts become thinner, drier, and darker in color; the tumors shrink in size, and then the crusts are detached at the circumference—this detachment increasing in extent as the granulomata gradually resolve. At last the wasted crusts fall off as dry scabs, and there are usually seen in place of the tumors slightly indurated circumscribed portions of skin of a lighter color than the natural hue. This condition, however, is transient. The induration rapidly disappears, and the light patch changes to a black macula which may take a considerable time to fade away. In a small proportion of cases, and more especially in the light-skinned races, the white patch persists for variable periods and there is no subsequent hyperpigmentation.

As soon as the macula is formed there is nothing whatever to indicate that a tumor formerly existed at the site. There is no induration or loss of substance; and, excepting the alteration in the pigmentation, the skin appears to be in a normal condition. Ordinarily the maculæ persist for months or even for years, but the author has seen them disappear entirely in a few weeks, and then all trace of the disease is gone.

Such, then, is the way in which the granulomata disappear by resolution in uncomplicated cases of yaws. But in debilitated subjects, and in those suffering from concomitant disease, more especially when the tumors have been subjected to injury or irritation, they break down into ulcers, which in the early stages are sometimes covered with yaws crusts. The ulcers are at first no larger in lateral extent than were the granulomata from the breaking down of which they have been formed, and they do not extend below the true skin. But in cachectic individuals and in those suffering also from malarial diseases, syphilis, or tuberculosis, and in those cases in which irritating dressings have been applied, they may spread deeply and widely until subcutaneous tissue, fascia, muscle, and bone are successively attacked. In such cases the ulcers sometimes become terribly and rapidly destructive to the surrounding tissues, and this is more especially the case when the patients have been brought to

a condition of mercurial cachexia or when the disease is complicated with syphilis or tuberculosis. After these large ulcers have persisted for some time they may cause the entire suppression of the yaws, which, however, remains latent in the system. If the ulcers be cured, the yaws will reappear and the disease will then run its ordinary course. In a certain number of instances, however, this disappearance of the eruption will be permanent and the ulcers will lose their infectiveness. When repressive measures were first instituted in Dominica, and when the worst cases of the disease were segregated in hospitals, it was found that severe ulcerations occurred in eight per cent. of the patients, but in every instance the ulcers were due to complications or to concomitant diseases, and therefore they could not be classed as actual attributes of yaws. After some years, when all the old and neglected cases had been drafted into the hospitals, such examples of extensive ulceration were less frequently seen. It has been asserted by some writers that the so-called "yaws ulcers" have certain diagnostic characteristics; but a careful examination of several hundred cases has led the author to the conclusion that when yaws is complicated by ulceration there is nothing in the lesion to distinguish it from one or other of the ordinary types of ulcers described in the text-books and seen in all parts of the world.

The *duration* of the uncomplicated disease varies considerably. It may last for weeks, months, or even years. The period, indeed, depends on idiosyncrasy, condition of health at the time of infection and afterwards, and treatment both hygienic and medicinal. In mild cases in vigorous subjects the granulomata will begin to be absorbed within six weeks of their formation, and in other instances they will remain without the slightest change for many months, no matter what may be the nature of the treatment. It frequently happens, too, that successive crops of the eruption are evolved during the course of the disease. This, however, can be described as a secondary eruption only in point of time, as there is nothing whatever to distinguish it from the eruption as it appeared in the first instance. As many as six crops of the eruption have been recorded, and they are each usually preceded by an elevation of temperature and other constitutional symptoms seen at the onset of the disease.

After the fever of the stage of invasion has subsided, there is ordinarily no marked deterioration of the general health. The appetite will be good, the sleep unbroken, and the spirits unaffected. But there is always a disinclination to work or to take exercise, and careful observation will show that there is some debility which may progress, in a certain proportion of the cases, to unmistakable cachexia.

The two principal indications, besides the initial fever and the

cachexia, of the constitutional nature of the disease are the enlargement of the lymphatic glands and the pains in the bones and joints.

Adenopathy.—It will be noticed at times that the femoral, inguinal, and cervical glands are tender, and in a certain number of cases they will become greatly enlarged and very painful. The femoral glands are most often affected in this way, and next in order of frequency come the inguinal and cervical and other lymphatic glands that lie close to the surface.

An examination by the author of 750 cases of the disease admitted to one of the Dominica yaws hospitals showed that in 39 instances, that is in 5.2 per cent., there was marked cachexia; and the absorbent glands were found to be greatly enlarged in 28, or 3.7 per cent., of the cases.

It has been already pointed out that *rheumatic pains* of the bones and joints may precede the eruption and persist for some time afterwards. Occasionally, however, these pains come on at later periods, and then they are usually very severe, more especially at night-time. They are, indeed, a well-marked symptom of the disease, and they are known as the "yaws pains." At times they are intense and even agonizing, so that sedatives have to be administered to mitigate them.

Itching is a common symptom in yaws, and it may be so severe as to give rise to distress. It begins as the maculæ evolve, and it persists through the papular stage; when, however, the granulomata are formed it subsides.

Relapses.—It is only within the last ten years that a more careful study of the disease by medical men in charge of West Indian yaws hospitals has established the fact beyond cavil that the malady in a certain number of cases is liable to relapse. In the Dominica yaws hospitals the percentage of relapses has varied from 3.6 to 5; but in similar institutions in other West Indian colonies the proportion has been considerably higher. In Nevis no less than 18.1 per cent. of the patients discharged as cured were readmitted after varying periods. The following notes of a case treated in one of the Dominica hospitals illustrates very well the relapsing nature of the disease:

V. S——, aged 16; negro. Admitted to the Central Yaws Hospital on July 2d, with extensive ulceration at the back of the left ankle, the former site of a "mother yaw." The ulcer is foul and deep with thick, everted edges. There are granulomata around the ulcer. Encrusted granulomata are scattered about the buttocks and legs, and there are some papulæ—"pian gratelles"—on the face. He has been ill for five months. He was first treated in the hospitals with calx sulphurata; and afterwards, as there was some cachexia, a mixture of quassia and iron was prescribed. He was fed well with eggs and milk and fresh meat and fish. The leg was elevated, and to

the ulcer was applied a carbolized linseed-meal poultice. On August 5th, he was much better in general health and the granulations of the ulcer were nearly level with the skin, but a fresh crop of granulomata appeared on the arms and body.

August 18th. Another crop of granulomata on the arms and buttocks.

August 26th. Yaws "drying up." Healthy granulations of ulcer level with the skin. Ordered iodide of potassium.

November 4th. After the last record he apparently recovered completely; the ulcer healed and there were no evidences of the disease. But he has now a general eruption of small granulomata. Ordered calx sulphurata again.

November 11th. Granulomata disappearing by resolution.

November 20th. A fresh crop of granulomata has appeared. The ulcer has broken open again. Iodide of potassium and tonics prescribed. From this time no fresh granulomata were evolved, but the ulcer healed very slowly. He was discharged cured on July 26th of the following year after a stay of a little over twelve months in the hospital, and he had no return of the disease.

Relapses may occur at any time within six months of the apparent cure, and in a small proportion of cases there may be a second or even a third relapse.

A curious and noteworthy fact in connection with yaws is that any profound impression made on the system by an attack of *intercurrent acute disease*, or even by a sudden chill giving rise to congestion or inflammation of some internal organ, has oftentimes the effect of producing in a very brief period the complete absorption of the characteristic tumors. In certain instances the symptoms in this way disappear never to return, but in most cases the eruption is thrown out again at varying intervals after the cure of the intercurrent disease. This fact of the retrocession of yaws was observed by the earlier writers, who alluded to it as the "repulsion" of the disease by measles, smallpox, etc. The author has seen the yaws so "repelled" by attacks of dysentery, remittent fever, and measles, and by profuse ptyalism, to reappear when these conditions were recovered from.

It has been asserted that vaccination protects from yaws as much as from smallpox. In order to determine this question, the author inquired carefully into the matter, and vaccinated a number of unvaccinated yaws patients, with the result that the assertions were found to be not in accordance with fact, for vaccinated persons are just as liable to contract yaws as the unvaccinated, and the disease is neither modified by nor does it modify in any way the course of vaccinia.

Immunity.—The early authorities on yaws taught that one attack of the disease invariably established in the system a complete immu-

nity from further attacks, but later writers brought forward facts to show that this was not always the case, and, now that the malady has been more carefully studied, it is found that second infections are fairly common. This matter was one of the questions that engaged the attention of the author when he was commissioned by the English Government, in 1891, to inquire into the prevalence of yaws in the West Indies. As the result of the inquiry the truth of the following propositions was established:

I. That one attack of yaws does not always give immunity from a second attack.

II. That the immunity afforded by an attack of the disease is, in many instances, if not in all, lessened by lapse of time.

III. That the immunity in some persons totally disappears after several years.

IV. That the manifestations of the second attacks of the disease do not vary in any essential particular from those of the first attacks.

Diagnosis.

The attributes of yaws as given in the preceding section are such as to render its diagnosis comparatively easy. It has, however, often been confounded with syphilis and tubercle of the skin; and, even now, a few writers assert that it is either syphilis pure and simple, or a syphilitic disease produced by the long influence of race and locality. Yet it is proper to point out that most of those who still maintain the theory of the identity of yaws and syphilis have had no personal experience of the former disease, and they have doubtless been misled by the many erroneous accounts of so-called "later manifestations" or "tertiary symptoms" of yaws, which are nothing more or less than manifestations of concomitant diseases quite distinct from the original attack of yaws. These errors of diagnosis have originated and been perpetuated by assuming, often on the *post hoc propter hoc* line of reasoning, that various chronic and destructive forms of ulceration are attributes of yaws, whereas the disease is a non-ulcerative one, and its cutaneous lesions disappear without leaving any cicatrix. Indeed, this is one of the great diagnostic signs of yaws, and it at once separates the malady from syphilis and scrofula, the lesions of which leave scars behind them.

Tuberculosis.—Both lupus and scrofuloderma are fairly common in the West Indies, and both these cutaneous forms of tubercle have been confounded with yaws. Numbers of cases have come under the author's observation in which tubercle of the skin and yaws have occurred in the same individual, but there has been no difficulty in

diagnosing the coexistence of the two diseases when the yaws has appeared as the secondary affection, inasmuch as at the margins of the ulcers the granulomata become developed, and the characteristic yaws eruption usually appears in other situations. But the combination of the two diseases is a serious one, and constant relapses of the yaws are the rule. Indeed, few of the patients become permanently cured. Owing to mistaken notions of the attributes of yaws, many cases of scrofuloderma alone have been admitted to the yaws hospitals, and the primary disease has been aggravated after a time by the infection of the ulcers with the yaws virus. Tuberculosis has the property of remaining latent in the system for considerable periods, and the foci may be aroused into action by the accession of acute disease. This property often accounts for scrofulous ulceration and lupus supervening on yaws; and it serves to explain why such forms of ulceration have been set down as later or tertiary symptoms of that malady. An examination of 2,397 patients under treatment in yaws hospitals in Dominica showed that 119, or rather less than 5 per cent., were subjects of some form of tuberculosis of the skin.

Syphilis.—From the earliest times of which we have any written account of yaws, the disease has been confounded with syphilis; and even now their identity is believed in by a few persons of eminence, notwithstanding the fact that all medical men who have had considerable experience of yaws become satisfied that it is a disease sui generis. It does not appear, however, to have suggested itself to many observers that yaws and syphilis might be concomitant in the same individual, and that the attack of the former disease might cause the outburst of the latent tertiary symptoms of the latter. But this is what actally occurs in a number of cases, and usually the so-called "tertiary symptoms" of yaws are really nothing more than the manifestations of tertiary syphilis in persons affected with yaws. Syphilis is a common disease in all the West Indian islands, and it would be strange indeed were the two maladies not at times to be found in the same individual. In those cases of yaws in which chronic, intractable, and destructive ulcerations came on, the explanation lies in the fact that there is a complication with tubercle or syphilis. It may not always be easy to determine at first what is the exact nature of the complication, but by patient and careful observation the difficulties of diagnosis will disappear. It is not possible in the space allotted for this article to enter fully into this subject, but the author has done so elsewhere, and those who desire to follow up the question may be referred to the report of the West Indian Yaws Commission.

The theory advanced by Jonathan Hutchinson that yaws may be

a syphiloid disease produced by the long influence of race and locality is disproved at once by the fact that syphilis in all its typical forms exists now, and has existed for many generations, amongst the races most subject to the ravages of yaws. Syphilis is the same disease amongst them now as it was then; time, race, and locality not having altered any of its manifestations.

The diagnosis between yaws and syphilis is easy to those who have had any experience of the two diseases. And even Mr. Hutchinson, who inclines to the belief of their identity, is forced to admit that "all the more recent observers who have studied the malady in its native haunts are, I believe, unanimous in the opinion that it is not syphilis." The essential points of diagnosis may be stated briefly as follows:

I. Yaws is confined to the tropics, whilst the distribution of syphilis is universal.

II. In the large majority of cases yaws occurs in children, whilst acquired syphilis is a disease of adult life.

III. The fœtus in utero is never affected in yaws as it sometimes is in syphilis.

IV. Yaws is not hereditary, and syphilis commonly is so.

V. The offspring of persons affected with yaws never have "Hutchinson's teeth," which is a frequent manifestation in children of syphilitic parents.

VI. The chancre is never seen in yaws—which has no "primary sore" of any kind.

VII. Micrococci are found in the affected tissues of yaws, and they are absent in those of syphilis.

VIII. The sore throat of syphilis is never seen in yaws.

IX. There is no alopecia in yaws as in syphilis.

X. Itching, which is not present in syphilis, is a frequent and troublesome symptom in yaws.

XI. Iritis, which is not unusual in syphilis, is never seen in cases of yaws.

XII. The eruption in syphilis is polymorphous, whereas in yaws it is constant in character—the squamæ and the papulæ being simply earlier and undeveloped forms of the granulomata.

XIII. In yaws, should the eruption disappear and break out again, no matter after what interval of time, it is the same characteristic granulomatous one that has evolved through the stages of squamæ and papulæ; whilst, should an eruption disappear in syphilis, another eruption of an entirely different form and character may break out, and the nature of the new eruption cannot be known until it appears on the skin.

XIV. In yaws the macule is dark, in syphilis it is copper-colored.

XV. The mucous membranes are frequently affected with eruptions and ulcerations in syphilis; but in yaws it is extremely rare for the eruption to be seen in such situations except when due to the extension of an enlarged granuloma from the skin in the neighborhood, and ulceration of the mucous membranes is never seen in uncomplicated cases of yaws.

XVI. In yaws there are no gummata or nodes, and there are no lesions of the nervous system, or implication of the internal organs, as in syphilis.

XVII. Yaws is essentially a non-ulcerative disease, the granulomata disappearing usually by resolution and leaving no scars behind them. In syphilis, on the other hand, ulceration is a common symptom of the malady; and scars, indicating destruction of tissue, commonly succeed the eruptions.

XVIII. There is no eruption in syphilis identical with that so characteristic of yaws. The only one that approaches it in appearance is rupia, which, when fully formed, is a shallow ulcer covered with a dark, conical, laminated crust, whereas the mature yaws eruption is a cutaneous tumor topped with a yellowish unlaminated cap of inspissated secretion.

XIX. Cutaneous eruptions in syphilis are secondary forms of the disease, whilst in yaws the eruption is the primary and only local manifestation.

In regard to this question of diagnosis, Imray—one of the highest authorities—states that yaws "is also *essentially primary*, that is, it cannot be considered as the result of a previous disease of a different form. It has one primary form, and runs one regular and certain course, unless affected by constitutional peculiarity, or complicated by previous disease in the system, or aggravated by neglect. Syphilis prevails in most of its forms, both primary and secondary in these countries very much as elsewhere, but I have never met with an instance, nor have I heard of one where the characteristic eruption of yaws has occurred as the result of a primary syphilitic sore, in short, as a secondary symptom of syphilis. If syphilis and framboesia exist side by side, as it were, among the same people, and that for a long period, perhaps two centuries, it is surely very remarkable that they should remain separate if identical in nature and origin, that we never find the one occurring as a sequel of the other, that the one can always be readily diagnosed from the other. It must also be remembered that the negro races are quite as susceptible of the action of the syphilitic poison,

and suffer from it the same disastrous consequences as the white races."

Parangi.—This disease, which occurs in Ceylon, was the subject of a government investigation conducted by Sir William Kynsey, the result of which was published in 1881 under the title of "Report on the Parangi Disease of Ceylon." The disease was thought by some observers to be yaws, and subsequent writers have assumed that the question of identity has been established, and roundly assert that Ceylon is one of the endemic foci of yaws.

The incubation period of parangi, which is not marked by any recognizable symptoms, extends from two to eight weeks. The stage of invasion is ushered in by fever, which lasts from two to eight days, and is followed by the eruption of papules, like those of acne or lichen, which may terminate in resolution with desquamation and pigmentation of the skin, or may proceed to ulceration. In the latter case the papules enlarge, suppurate, and form a crust, under which ulceration goes on. The ulcer is clean and healthy; and the crust, if removed, is not reformed. When the disease terminates by resolution, the ulcers heal and pigmented cicatrices mark their sites. Should the eruption attack the soles, a condition known as "dumas" occurs. Kynsey described this as follows: "The horny cuticle protrudes and becomes very painful, and in a short period ruptures and gives egress to a fungoid growth covered with a dirty yellow scab. This fungoid growth consists of hypertrophied papillæ and fibrous tissue." In the later stages of the disease terrible ulceration involving muscle and bone may take place, the unhappy sufferers become emaciated and deformed, and finally they are usually carried off by some inflammatory disease.

On comparing these symptoms with those of yaws it will be seen that they are widely different. The chief diagnostic sign of parangi, and one that at once separates it from yaws, is that of ulceration. Parangi appears to be essentially an ulcerative disease, whilst yaws is not; besides which the yaws granuloma, which is seen in every case of the malady, is absent in parangi. It is true that the "dumas" bears a resemblance to the "tubboe"; but, as has already been shown, tumors similar in appearance to tubboes may occur in persons in the West Indies who have never had yaws. In fact the condition is produced principally by mechanical agencies; for any kind of circumscribed growth from the dermis pushing its way through the leathery cuticle of the sole of one who walks barefooted in the tropics is likely to give rise to the train of symptoms seen in tubboe and dumas.

It is evident from Sir William Kynsey's report that under the

term parangi are included several diseases, amongst which may be mentioned syphilis, tubercle of the skin, and the so-called "oriental sores."

Prognosis.

Yaws is a chronic disease producing more or less debility, which is usually aggravated by the defective diet and the mal-hygiene of the people amongst which it most prevails. But unless it be associated with some other constitutional disease, it rarely terminates fatally. It has the property of lighting up any latent tendency to tuberculosis, more especially the scrofulous and lupoid forms, and the concurrence of the two diseases often gives rise to fearful states of ulceration and deformity. And similar conditions are produced by the existence of yaws and syphilis in the same individual.

In an uncomplicated case recovery under appropriate treatment may be hoped for in from two to six months without any after deterioration of the general health. The experience of the author, however, shows that the disease is more severe and takes longer to cure in adults than in children, and that during the period of adolescence and the years immediately succeeding it, the attacks of yaws are of a more protracted nature.

It is a noteworthy fact that the mortality in the West Indian yaws hospitals has been on the average a very low one. In the twenty years, from 1871 to 1891, there were 7,157 patients under treatment in these institutions; and of this number 185 died, which gives a mortality of 25.8 per thousand, which is a lower death rate than that of some of the colonies. And of this number only a small proportion died of yaws, the greater number of deaths being due to concomitant disease. The low mortality in the yaws hospitals is owing in a great measure to the fact that the patients are better fed, better clothed, and placed under better hygienic conditions than they are in their own homes.

Histology and Pathology.

In considering the histology of the disease it will be convenient to describe the characteristic tumor in its various stages of development from the squama, through the papula, to the perfectly formed encrusted granuloma. As, however, yaws is most often seen in the dark-colored races, the appearances described will be those observed in the disease in the negro, whose skin is rendered dark by the melanin granules of the pigment cells which infiltrate the upper part of the dermis and the two lower layers of the epidermis. These cells

are found in greatest abundance in the rete Malpighii, they are round or oval in shape, and they measure from 4.9 μ to 7.3 μ in diameter.

The Squama.—The epidermis is increased in thickness, and the surface of the horny layers is irregular by reason of the flaking off of portions of the affected area. Towards the circumference of the patch the horny layer separates into strata and presents a ragged appearance. About the centre of the patch, the cellular débris is heaped up in masses in some places, and the horny layer almost entirely disappears in others, the rete Malpighii—which is proliferated—being nearly exposed. The pigment cells are enlarged, they

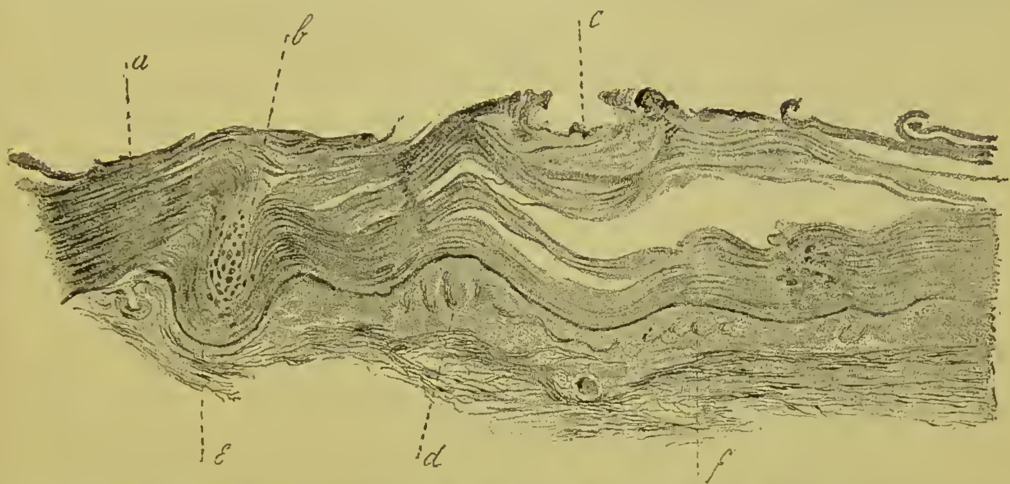

FIG. 15.—Vertical Section of a Squama in the Sole of the Foot. × 26. *a*, Greatly thickened horny layer of the epidermis; *b*, a cuticular grain showing how it has been formed by involuted strata of the horny layer of the epidermis; *c*, a pit from which a cuticular grain has escaped; the pit is partly worn away and it is being flaked off; *d*, enlarged papilla; *e*, a portion of the dermis from which the papillæ have disappeared, probably from the pressure of the cuticular grain; *f*, papillæ reforming under the pit from which the cuticular grain has escaped.

increase from 7 μ to 10 μ in diameter, many of them become polygonal in shape, and they infiltrate the whole of the rete Malpighii and are especially numerous over the papillæ.

The dermis is very vascular and thick and the papillæ become enlarged at the circumference of the squama, but they disappear towards the centre, the lower pigmented cells of the epidermis running in a wavy line over the flattened dermis. Under the heaped-up masses of cellular débris, however, the papillæ are enlarged, being widened at the bases and rounded at the summits. Islets of granulation tissue are seen between the bands of fibrous tissue, and they are more abundant in the neighborhood of the hair follicles and blood-vessels. Those follicles included within the squama are much dilated at the exit of the hair. They are, in fact, funnel-shaped, and the widened portions are filled with epidermal scales and débris.

Micrococci, either singly or as diplococci, are seen in the débris,

the epidermis, and the hair follicles. These cocci measure from 0.5 μ to 1 μ in diameter. In stained sections portions of the exfoliating epidermis are seen to be darkened by colonies of cocci, which are set free by the shedding of the epidermal scales.

In squamæ of the sole curious oval "cuticular grains," as the author has elsewhere termed them, measuring on an average 0.056 mm. in length and 0.028 mm. in breadth, are seen to be enclosed in pits in the thickened horny layer. These grains are formed by a

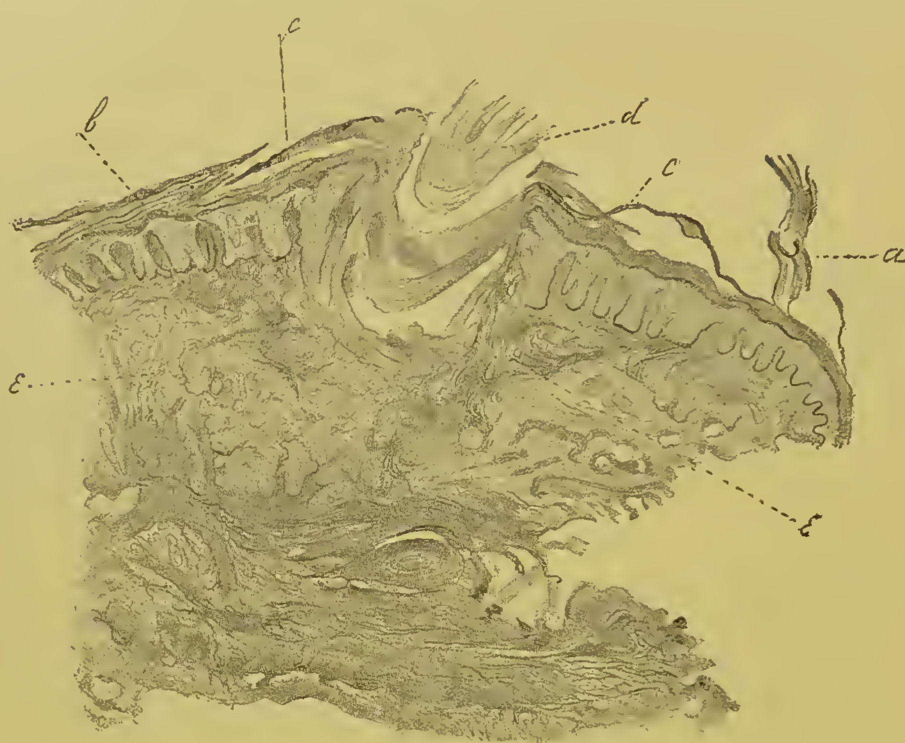

FIG. 16.—Vertical Section through the Centre of a Papula. × 26. *a*, Thickened horny layer of the epidermis flaking off; *b*, protoplasmic cells forming the deeper layer of the horny epidermis; *c*, *c*, enlarged papillæ; *d*, greatly dilated hair follicle with a portion of the hair in the centre; *e*, *e*, granulation tissue.

continued involution of circumscribed portions of the horny layer caused by the unequal proliferation of the lower strata of the epidermis. As the upper strata are exfoliated or worn away the involuted cuticle is left without attachment at the upper part, and then it presents the appearance of a pit contracted at its orifice and filled by an oval stratified body. Later on the cuticular grain becomes loosened, and its upper portion is worn away and becomes ragged or fibrillated owing to its stratified formation. It is eventually set free, and its pit is gradually exfoliated or worn away by friction in walking barefooted.

The Papula.—The papule is seen to begin at certain circumscribed

portions of the squama where there is increased proliferation of the cellular elements of the skin. The papillæ enlarge more especially towards the centre of the papula. The round cells of the rete Malpighii rapidly increase in number, and the pigment cells disappear, the melanin granules in those that are left becoming much paler. The horny layer is also increased in thickness, the cells of the lower layers are seen to be protoplasmic, and the upper layer shows the ragged appearance due to desquamation. In the recently formed papula the summit is destitute of an epidermal covering, the cuticle being replaced by cellular débris without any pus or secretion. The dermis is more infiltrated with granulation cells than in the case of the squama, and leucocytes pass out of the blood-vessels into the tissues; this migration, however, does not appear to occur to any considerable extent.

In those sections which include hairs the follicles are seen to be widely dilated towards the surface, the hair being surrounded with cellular débris and a yellow amorphous substance identical with the yellow inspissated secretion that forms the crust of the granuloma. After a time the hair falls out of the follicle, which becomes transformed into an oval cavity containing egg-shaped bodies composed of the inspissated secretion and entangled cellular débris. Colonies of micrococci are seen in all the layers of the epidermis, and in the oval bodies in the altered hair follicles.

The Granuloma.—The structure can best be seen in sections of one of the smaller granulomata. Under a low magnifying power it will be observed that the papillæ increase in size from the circumference to the centre, and that all the elements of the skin (except the horny layer) are infiltrated with masses of granulation cells, the summit of the tumor being covered by a crust formed of an inspissated yellow secretion in which are entangled a few red blood corpuscles and some cellular débris and foreign substances. In the smaller and recently developed granulomata all the cutaneous histological elements are easily recognized, but there is a proliferation of all the tissues, and after a time the granulation cells gradually invade and obscure all the normal structures.

An examination of a fully developed granuloma will show that the following changes have taken place in the skin.

At the circumference of the tumor the epidermis is thickened and the papillæ are enlarged; but on the tumor itself the epidermis has disappeared, its place being taken by the crust which overlies tho naked papillæ and dips down between them, forming interpapillary processes to replace those of the lost Malpighian layer of the skin. The papillæ, more especially those at the centre of the growth,

are enormously enlarged, many being club-shaped at their extremities and others being divided into lobes at their summits. Externally the papillæ are invested with a thin layer of fibrous tissue, and internal to this is sometimes seen a stratum of spindle-shaped cells which lies in contact with the granulation tissue of which the bulk of each papilla is almost entirely composed. The pigment cells are

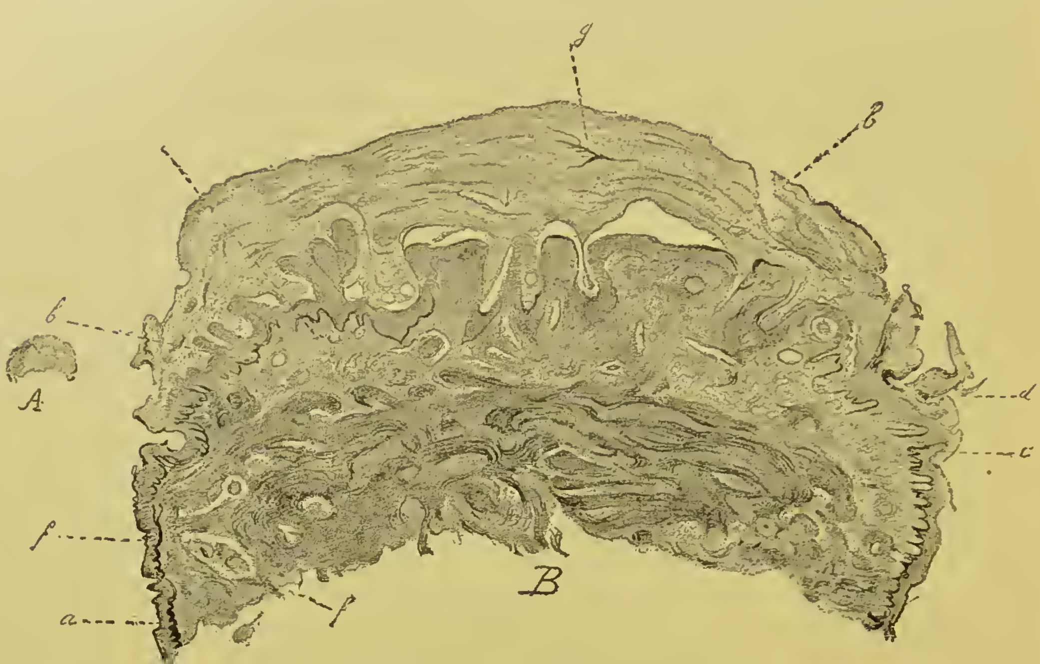

FIG. 17.—Section of an Entire Small Granuloma. *A*, Natural size; *B*, magnified 10 diameters; *a*, unaffected skin at the margin, showing the natural size of the papillæ; *b*, *b*, papillæ gradually enlarging from the circumference to the centre of the granuloma where they attain their greatest development; *c*, the termination of the proliferated epidermal tissues and the beginning of the crust which replaces them over the tumor; *d*, large masses of the micrococci; *e*, granulation tissue that has invaded and caused enormous enlargement of the papillæ; *f* section of a hair showing unaltered pigmentation; *g*, a blood stain in the crust.

very numerous in the skin at the circumference of the tumor, and they contain a dark nucleus and many melanin granules. At the periphery of the tumor these cells are still seen in places in process of disintegration, the melanin granules being set free in the tissues, to be thrown off later on with the secretion which builds up the crust. The granuloma itself is entirely free of pigment cells or of pigmentation, no matter how dark may be the skin of the subject. The dermis is infiltrated with granulation cells, and there is a proliferation of the fibrous tissue which appears as thick anastomosing bands. Between these bands are islets of granulation tissue which increase in size towards the bases of the papillæ. The granulation cells areround in outline, they contain one large nucleus, and they vary in diameter from 6 μ to 9.6 μ. Charlouis describes the merroneously as colorless

blood corpuscles that had escaped from the vessels and accumulated extensively in the cutaneous tissues. The blood-vessels are enlarged and numerous, and in the hypertrophied papillæ small vessels are observed to have taken the places of the capillary loops.

Micrococci are seen in abundance in the upper parts of the tumors, and zoogl*œ*a masses, or colonies, of them are to be found in the papillæ and in the dermis, where they are surrounded by granulation cells.

The evolution of the granulomata has been described by inaccurate observers as that of a pustulotubercular eruption, and this error —which has been widely copied by inexperienced writers—has given rise to a mistaken view of the attributes of the disease. If cover-glass specimens of the secretion of the granulomata—obtained immediately after forcible removal of the crusts—be carefully examined, round cells averaging 4.8 μ in diameter will be seen. These are

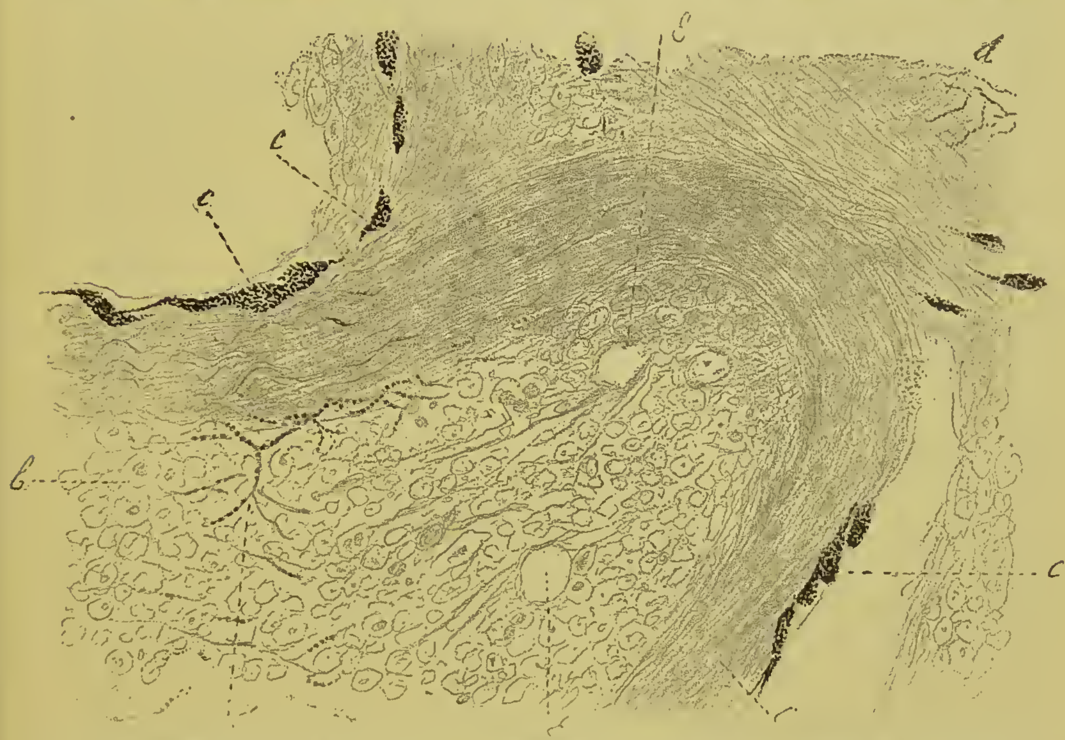

FIG. 18.—Oblique Section of a Portion of a Granuloma. *a*, A portion of a crust that has replaced the interpapillary process of the epidermis; *b*, granulation tissue of the papilla; *c*, *c*, *c*, colonies of micrococci; *d*, *d*, melanin granules; *e*, *e*, arteries in section. × 300.

smaller than pus cells and they do not contain large nuclei dividing by fission. They are not pus cells as they have been held to be, but simply the granulation cells of which the bulk of the tumor is formed.

Of course, if a granuloma be irritated or injured suppuration may occur; this, however, must be considered not as a symptom but as a complication of the malady.

When the eruption terminates in resolution, the granulation cells gradually disappear, the papillæ decrease in size, and they and the dermis are seen to be free of micrococci. The microbes, however, may be observed in the crust and amongst the desquamating epidermal cells at the circumference of the tumor. At first the lower stratum of the wasted crust is directly in contact with the papillæ, which continually decrease in size and lie close together. But after a time the crust begins to flake off and a new epidermis is formed by an extension of the protoplasmic spheroidal cells of the rete Malphighii in the neighborhood. Amongst these cells, later on, will be found pigment ones in abundance, so that the new epidermis over the site of the former granuloma, which was at first entirely free of pigmentation, rapidly becomes darkened until it is of a deeper tinge than the surrounding skin. In this way the macula in formed, and the reason why it is at first lighter in color, and afterwards much darker than the surrounding skin, is easily understood.

In the dermis may be seen numbers of multinuclear fibroblasts, smaller than the granulation cells which have disappeared; and the hair follicles that have escaped destruction assume their natural condition, the hairs in them being normal in appearance. The writer has never been able to make out any sebaceous or sudoriparous glands in the numerous sections he has examined, and it may be inferred, therefore, that these structures are the only ones that have been destroyed by the morbid process.

The Macula.—After the granuloma has disappeared the macula is the only indication of its former existence, and when this gradually fades away, there is nothing to show that a tumor or any other lesion has been present.

If sections of a macula be examined under a microscope it will be noticed that granulation cells and micrococci are entirely absent from the tissues. There is a proliferation of the pigment cells, indeed the lower layer of the epidermis and the contiguous portion of the dermis appear to be composed almost entirely of these cells. The papillæ are small, low, and flat-topped in some places, and in others they have not yet been re-formed after their collapse by the removal of the granulation tissue, so that the dermis runs along as a wavy or straight line. The dermis is infiltrated with fibroblasts, some of which are fusiform. In sections of maculæ in which the return to natural skin is more advanced, a larger number of papillæ are seen and they approach more or less to the normal form and structure.

The Internal Organs.—Owing to the low mortality of yaws patients it is not often that an opportunity is found of making a microscopic examination of the internal organs; and, as far as the author knows,

the only published account of such an investigation is the one contained in the report of the West Indian Yaws Commission. A patient having died of yaws in the Dominica Yaws Hospital whilst the author was engaged in the island in his work as Special Yaws Commissioner, a thorough examination of the body was made with the following results. The blood in the heart and vessels was found to be unaffected and free from microbes. But the yaws micrococcus was discovered in the absorbent glands, and in abundance in the fibrous investing capsules of the lungs, the liver, the kidneys, and the spleen, as well as sparingly in the tissues of the lungs and spleen contiguous to the capsules of these organs. Beyond some proliferation of these fibrous structures there were no abnormalities to be found. The yaws pains that are sometimes felt in the body and limbs of patients suffering from the disease are doubtless due to the hyperplasia of the fibrous tissues caused by the irritation of the micrococci in them. The blood does not appear to be affected at all, for numerous examinations of it have given negative results, and attempts to communicate the disease by blood inoculation have repeatedly failed.

Bacteriology.

In the year 1892 a careful investigation into the bacteriology of yaws was carried out in the Government Laboratory of Antigua by Mr. Francis Watts and the author, and the latter continued the work later on in St. Kitts and Dominica. A micrococcus was found invariably in the affected cutaneous tissues, and pure cultivations of the microbe showed that its microscopical characters were constant and that its macroscopical appearances differed from those of micrococci already discovered and described in works on bacteriology. As a result of their work, Mr. Watts and the author gave, in their joint report, the conclusions they arrived at in the following words:

"The results of our work in regard to this inquiry may be summed up as follows:

"I. A microbe, in the form of a micrococcus, was found constantly in the secretion from the granulomata characteristic of yaws.

"II. This microbe was successfully cultivated in nutrient media, and pure cultures were obtained to the third generation.

"III. The macroscopic appearances of the cultivated microbe may be described as white mucoid oval or rounded masses, with a chromogenic tendency, which, however, was not displayed so well in fluid media. The coloring-matter when present was, in most instances, of a salmon tint.

"IV. Under the microscope the microbe was seen to be a coccus,

from 0.5 to 1.5 μ in diameter. It occurred singly, or in twos, threes, fours, short chains, and zooglœa or small colonies. As the cocci multiply by transverse fission, this grouping in diplococci, triads, tetrads, and streptococci is merely accidental, and, where observed, is only indicative of the rapid growth of the microorganism.

"V. The microbe was found in abundance in the affected tissues of persons suffering from the disease, and no other pathogenic microbe was found in association with it.

"VI. In no instance was the microbe discovered in the blood, although it was successfully multiplied in the serum in drop cultures.

"VII. The microbe was found and successfully cultivated in Antigua, St. Kitts, and Dominica, and it occurred under identical conditions in these three islands.

"VIII. Inoculations into animals from the cultivations gave negative results, as did also inoculations from the secretion of the granulomata, by which Dr. Nicholls, some years ago, was able to communicate the disease to human beings. These facts, therefore, whilst they indicate that animals are probably immune, do not disprove the theory that the microbe is pathogenic.

"IX. In the absence of the concluding proofs of the pathogenesis of the microbe, namely, the production of the disease in a healthy animal by inoculation of the pure cultivations, and the after discovery of the microorganism in the fluids or tissues of the affected animal, we cannot positively declare that the micrococcus is the contagium of the disease.

"X. But, in view of the facts we were able to establish, and tho subsequent discovery by Dr. Nicholls of the microbe in the lymphatic system, and in various organs of a patient who died of yaws, we are of opinion that the micrococcus is the cause of the disease, and that it invades the system through the lymphatics."

Subsequent to this investigation the author preserved some dust swept up from the yaws hospital in Dominica in a box in a dry place for over three months and then inoculated it into nutrient media, with the result that the micrococcus grew more vigorously than when it was obtained in cultures from the affected cutaneous tissues. Assuming, therefore, the micrococcus to be the cause of the disease, the mode of infection and the clinging of the contagion to huts and localities aro readily explained by these experiments.

There has existed a difference of opinion amongst writers on the disease as to whether yaws is a local or a general malady, and the clinical histories of a number of cases will furnish apparently conclusive evidence on both sides of the question. The fact is that both theories are correct, for the pathological investigation the author has

had the good fortune to carry out under government auspices brings the widely divergent theories into harmony.

It is clear that the disease is due to the morbid influence of a microbe, and accumulated evidence tends to show that the "yaws micrococcus" is the microbe in question. Nature uses every effort to isolate the pathogenic organisms by building up cellular barriers which confine them to certain points, and so prevent a general invasion of the system by them and the consequent diffusion of their metabolic products. Should this process continue in an effective manner, the microbes are destroyed and the harmful action of their toxins is limited, or the disease is held in check for a sufficient length of time to enable immunity to be developed. If, however, this struggle against the microorganisms languishes by reason of ill health, or if the cellular barriers are broken down, a general infection of the system takes place, and the disease—which may be said at first to have been a purely local one—then manifests constitutional symptoms.

Treatment.

An uncomplicated attack of yaws in an otherwise healthy individual tends to spontaneous recovery. This fact was noted by Williamson in 1817, subsequent writers have insisted on it, and a number of cases have come under the author's observation in which the disease has terminated in resolution without any medicinal treatment whatever.

A consideration of the pathological facts given in the previous section indicates in a general way the line of treatment that should be adopted, for there is no specific known for yaws, the much vaunted power of mercury to produce a certain cure in all cases having been shown to be mythical by the large experience of many medical men.

The disease is a chronic one, and any interference with its course is likely to do more harm than good. It has therefore to be guided to a cure, the indications being to strengthen the constitution in every possible way in order that the vital influences at work to neutralize the morbid processes may be kept at their full vigor. To this end the anæmia so prevalent in tropical climates must be counteracted by ferruginous tonics, and intercurrent disease when present must be cured if it be possible to do so. Digestive troubles must be removed. Irregularities of the excretory and other organs must be set right. And proper sanitation, good food, and adequate clothing must be assured.

It often happens that yaws patients, who as a rule come from the lowest and poorest sections of the people, are in a debilitated condi-

tion, or are subjects of some intercurrent disease. If such be the case, it is useless to attempt special treatment until the patients have improved in general health. The practice of the author in these cases is to disregard the yaws for a time and to direct attention to the other troubles, and extended experience has shown the advantage of such a line of procedure.

At the early stage of the disease those drugs that favor the efflorescence of the cutaneous eruption should be administered; for, if there be any interference with the formation of the granulation tissue—that is with the cellular barrier—the microbes will be set free to work mischief in the system. The general health will then be greatly deteriorated, any latent disease will rapidly develop, and the yaws—which may for a time have disappeared—will break out with increased virulency. Hillary alludes in his work to what he calls the "vile custom" of the "surgeons of the Guinea ships" in repelling the disease on its first appearance so that the slaves might be landed with a clean skin and sold at a high price to planters, who found after a time that the yaws appeared in so severe a form as to be very difficult of cure or even incurable.

In order to favor the throwing out of the eruption a vigorous cutaneous circulation is necessary. And this explains how chills produced by cold baths early in the morning or late in the evening, by wearing insufficient clothing, by living in damp huts, and by exposure to the inclemency of the weather, cause frequently a sudden disappearance of the eruption with a certain manifestation of the disease later on. The recorded experience in the West Indies shows that serious relapses are very frequent when the granulomata are destroyed early with caustics. In the last stages of the disease, however, should several of the tumors persist for a long time they may be destroyed without danger, for it will then be found that owing to inflammatory changes a permanently organized tissue has replaced the mass of granulation cells of which they were originally formed. But it is only in a very small proportion of cases that it will be found necessary to apply cauterizing agents to the tumors, for inflammatory changes result in them only from injury or continued irritation.

So as to promote the efflorescence of the eruption, diaphoretic and diuretic medicines should be at first administered, and then confection of sulphur should be given for several weeks. The action of sulphur on the skin, when the drug is taken internally, is to stimulate the cutaneous circulation, thereby relieving congestion and assisting in the repair of lesions and the absorption of damaged tissue. A good cutaneous circulation is also necessary for the proper formation of the granulation tissue, which, as has been seen, acts as a bar-

rier to cut off the microbes and to neutralize their harmful influence. Sulphur acts also as a mild laxative, stimulating the whole course of the alimentary canal. All these actions, being of benefit in the treatment of yaws, explain why the empirical use of sulphur in the olden days was found to be of so much benefit. During this time warm baths with a plentiful use of carbolic soap are to be recommended; indeed, when possible, such baths should be taken frequently during the whole course of the disease. Sea bathing is also very beneficial; and if the bath be taken when the sun is up, the sea will be pleasantly warm. Cases have come under the author's notice in which persons have been cured of yaws by frequently bathing in the sea and at the same time taking copious draughts of sea water.

In some few instances it may be found that no appreciable benefit is derived from the administration of the combination of sulphur and cream of tartar, and then calx sulphurata or calcium sulphocarbolate, together with vegetable tonics, may be given advantageously. What would appear to be very large doses, that is from two to four or even five grains, of the sulphurated lime should be administered; for such small quantities as gr. $\frac{1}{10}$ to 1, mentioned as usual doses in posological tables, are useless. In the author's practice no irritant effects on the stomach have been noticed from these seemingly big doses of the drug.

When the eruption has matured and lasted for some weeks, and not before, medicinal agents may be given to cause the absorption of the cutaneous tumors. But, as a rule, the disease is very chronic in its course; and the treatment, therefore, has to be persisted in for some time.

There is a diversity of opinion as to what these medicinal agents should be. The author, whilst acting as Special Yaws Commissioner in the West Indies in 1891, instituted inquiries amongst the medical officers as to the drug or drugs they employed in the treatment of the disease, and the following table shows the proportion of medical men using the six drugs indicated:

Mercury	41.5	per cent.
Iodide of potassium	36.6	"
Iron	36.6	"
Arsenic	26.8	"
Sarsaparilla	14.6	"
Sulphur	4.9	"

Some of the medical officers gave the names of several of the above-mentioned drugs in their replies. Thus mercury and iodide of potassium, or mercury and iron were often used together, as

were also arsenic, mercury, and iodine in the form of Donovan's solution.

Mercury.—Corrosive sublimate and Donovan's solution (liquor arsenii et hydrargyri iodidi) appear to be the favorite forms for administering mercury, but Plummer's pill (pilula hydrargyri subchloridi composita [B. P.]), and the red and the green iodide are often employed.

Although the literature of the disease shows that several far-seeing writers pointed out the evils of mercurialization in its treatment, it was the custom until recent years to dose all yaws patients with mercury. An accumulation of painful evidence is on record of the mischievous effects of this routine treatment, and the so-called "sequels of yaws" and "tertiary symptoms" such as anæmia, ulceration of the mouth and fauces, emaciation, etc., were for the most part the results of ptyalism and mercurial cachexia produced by large and repeated doses of the drug. Maxwell, in 1839, wrote as follows on this point: "Having frequent opportunities of watching the progress of yaws, as it was treated by mercury and when left to itself, I soon perceived that the exhibition of this mineral in any of its preparations possessed a temporary influence in repelling the eruption; but the number of fatal cases which followed its use, and the lamentable consequences to which the wretched patient was doomed, induced me to look upon mercury as an exceedingly dangerous and destructive medicine in the treatment of yaws, and I abandoned its use in every case, and have no reason to regret my determination." Similar evidence was borne by Wright, in 1791; by Williamson, in 1817; by Dancer and by Thomson, in 1819; by Boyle, in 1831; and by Robertson, in 1836. Of the medical practitioners in the West Indies at the present day, Drs. Paulin Orgias, of Grenada—who has had the direction of a yaws hospital for many years, and W. J. Foreman, of St. Kitts, who has had much experience of the disease as a district medical officer in that island and in Dominica and Tortola, are emphatic in their opinion that no mercury should be used in the treatment. The author, who has treated within the last twenty-five years over three thousand cases of yaws, in the early part of his hospital practice dosed all his patients with mercury, as many authorities recommended; the results were so unsatisfactory, however, that he had to abandon the system, and he now prescribes the drug in only a certain number of cases. The report of the West Indian Yaws Commission showed that those medical officers who employed the mercurial treatment were not more successful than those of their brethren who discarded it, indeed the statistics showed that the latter had a smaller proportion of relapses to deal with than the former.

Mercury has undoubtedly a curative influence on the disease, but it should never be given to the extent of producing ptyalism. The alterative effect is alone needed, and that may be secured by small doses of corrosive sublimate or Donovan's solution, and it is better to combine the former with some preparation of iron to counteract the anæmia produced by the drug. The usual prescription of the author, in those cases in his hospital practice in which he considers the administration of mercury advisable, is as follows: Corrosive sublimate gr. $\frac{1}{12}$ and tincture of the perchloride of iron ♏x., with glycerin and infusion of quassia, the draught to be given twice a day, and the effects are directed to be carefully watched so that no salivation may be produced. It is found that mercury is most useful in cases in which, in the later stages of the disease, the granulomata do not mature but remain as squamæ or papulæ. Even in these instances it sometimes fails to produce any beneficial results, and then an arsenical mixture may be administered with success.

Iodide of Potassium.—This drug appears to have been first used as a curative agent in yaws by Robertson, in 1836, who records its beneficial effects in cases that the failed to cure with mercury—which drug, he says, produced only "a temporary benefit, the disease always relapsing." The author has had a large experience of iodide of potassium in the treatment of the malady, but he finds that it is harmful if given in the early stages. Concerning the drug, Lauder Brunton states that "the iodine set free from the iodide is taken up by the albuminous substances, and the entrance of the iodine molecules into their composition causes them to undergo more rapid metamorphosis." A consideration of the pathology of yaws indicates at once how the administration of the drug would be injurious when the granulomata are forming, and how it would be of benefit in helping to remove the barriers of granulation cells when they had performed successfully the work for which they were massed together.

Arsenic.—The employment of arsenic was first suggested by Cazenave, in 1828; but it was first used, the author believes, by Mr. M. P. Duke, some time medical officer of one of the Dominica Yaws Hospitals. It is especially useful in chronic and abortive forms of the eruption, such as squamæ and papulæ, which often persist for long periods in spite of treatment. Its metabolic action on the epidermis is useful in occasioning the throwing-off of affected epidermal cells, and the rapid generation of fresh and healthier ones. Liquor arsenicalis or Fowler's solution is the form of the drug usually administered, and in most cases it may advantageously be combined with

citrate of iron and ammonia. Or the hydrochloric solution of arsenic may be given with tincture of the perchloride of iron, spirit of chloroform, and glycerin.

Iron.—Treatment by iron appears to have been employed in the first instance by Mason, in 1831, and since his time it has been a favorite remedy. As iron is a normal constituent of the body, in small doses it is a food as well as a medicine. Owing to the malnutrition of most of the poorer natives of tropical countries they are nearly all sufferers from anæmia, and many of them are subjects of ankylostomiasis. Ferruginous tonics are therefore indicated in nearly every disease from which such people suffer. In the yaws hospitals in Dominica iron in some form has been usually prescribed with a bitter vegetable tonic in the early stages of the disease, and such treatment has been followed by beneficial results.

When the treatment by mercury or iodide of potassium has been persisted in for some weeks, or even months, it will sometimes be found that the disease is pursuing so chronic a course that little or no effect appears to have been made on it, and then often much benefit may be secured by causing the patients to undergo a second course of confection of sulphur, so that the cutaneous circulation may be stimulated. In a certain proportion of cases in which this treatment is adopted a fresh crop of granulomata will be thrown out, and after a time the patients will rapidly progress towards recovery. In other instances the eruption—which has remained stationary—will begin to show signs of decline, and these cases too will progress satisfactorily. But some few patients will not do well, none of the remedial agents apparently having any effect whatever on the disease, and then ferruginous and other tonics are indicated, unless concomitant disease be detected when its special treatment becomes imperatively necessary.

In the great majority of cases local treatment is harmful, for the evolution of the eruption should not be interfered with. The statistics of the practice of some medical men who invariably destroyed the granulomata by caustics show a large preponderance of relapses. Indeed one strong advocate of the cauterizing plan asserts that "the disease almost always relapses after a variable time." In the yaws hospitals in Dominica it has been the custom to apply weak carbolic oil to the eruption so as to prevent the exfoliation of infective débris from the cutaneous surface.

When the eruption aborts or persists for a long period the author has found the application of an ointment composed of soft paraffin and corrosive sublimate to be of great use, and the weak ointment of the nitrate of mercury may be employed for the same purpose and

used as an application to granulomata that remain after a long medicinal treatment.

In a certain proportion of cases it is found that some of the granulomata break down into ulcers owing to their accidental injury, to the operation of extreme debility in ill-nourished persons, or to the influence of concomitant disease. The indications then are to heal the ulcers as speedily as possible, and it will doubtless be found that the best procedure is to suspend the administration of the special yaws remedies in order to carry out a tonic plan of treatment, or to grapple with intercurrent disease. There is no such thing as a specific yaws ulcer. The ulceration that occurs sometimes is an accidental complication, and in no way a necessary symptom of the disease. Ulcers of all the various kinds described in the text-books are at times seen in yaws patients, as they are seen in persons suffering from other diseases. They may be treated with success according to general principles, care being taken to protect them from being infected with the yaws virus, and in this connection it must be remembered that the granulomata are autoinoculable.

The complications of yaws most often seen in the western tropics are syphilis and tubercle of the skin. The author has observed the combination of syphilis and yaws in most of the British West Indian islands; and, more often than not, the unhappy sufferers have been pitiable objects of deformity and disease. Tertiary syphilitic ulceration in yaws patients is often rapid and extensive, skin, fascia, muscle, tendon, and bone being successively laid bare and destroyed; and often no treatment appears to be of any use whatever. At other times the progress of the concurrent disease will stop, and some of the ulcers will slowly heal, only to break out again, however, elsewhere. The patients, indeed, are practically incurable. In several of these cases where limbs have been so eaten away and corroded by ulceration as to endanger life the author has amputated them; but in every instance, after a variable interval, the ulceration has again broken out virulently elsewhere to terminate fatally, or to render the patients shocking examples of incurable disease.

Prophylaxis.

It has been shown that there is no specific for yaws; but, as the disease in uncomplicated cases tends to spontaneous recovery, medical men will find no difficulty in curing the great majority of cases coming under their care. And satisfactory results may be obtained by different methods of treatment, provided there be no interference with the efforts of the system to combat the invading virus as shown

by the pathology. But, in yaws-infected countries, it is not sufficient to treat and cure cases of the disease; for it is the duty of medical men and persons placed in authority to do all they can to prevent its spread. It is highly contagious, and the contagion attaches itself to clothes worn and to bedding used by yaws patients. In respect of these matters, the following conclusions arrived at by the West Indian Yaws Commission may be usefully given here:

"No system of dealing with the disease can be considered as even approaching to efficiency that does not provide for:

"(*a*) The isolation as far as possible of infected houses.

"(*b*) The thorough disinfection afterwards of these houses, and the destruction or disinfection of the clothes and bedding used by the sick.

"(*c*) The demolition of the wretched hovels that are a danger to the public by reason of the clinging of the contagion to them.

"(*d*) The rigid enforcement in all instances of ordinary sanitary precautions."

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INFLAMMATION.

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INFLAMMATION.

The Pathological Vital Processes in Inflammation.

Inflammation is in its nature a local disturbance of nutrition associated with pathological exudations from the blood-vessels; it leads at first to tissue degeneration, but subsequently usually also to tissue proliferation. In inflammation, therefore, we have to deal not with a simple vital process, but with a combination of different pathological vital processes.

The cause of inflammation is always based upon noxious influences acting on the tissues from without or upon such as have originated within the body. The external noxæ consist of mechanical, thermic, electrical, and chemical influences and of infections; and the latter play the most important part in the etiology of inflammations.

Among the external noxæ that may produce inflammation the most prominent are circulatory disturbances—for instance, permanent or temporary arrest of the blood supply, or else hemorrhages—and the formation of substances exerting a toxic effect. Very often, too, an inflammation may be due to various noxæ, a fresh injury being added to an existing inflammation; for instance, a traumatic or thermic inflammation may be followed by an infection, or to an existing infection a second or third one may be superadded.

The external noxæ become active first at such points of the body as are accessible from without—the external skin, the mucous membrane of the intestinal tract, the respiratory passages, and the lungs, the efferent urinary canal, the sexual passages, etc.—and the inflammations thus caused may be grouped together as ectogenous. When noxæ—*e.g.*, bacteria—are carried away in the lymph stream from their point of access to the body into the blood current, and in this way produce their effects in other regions, metastatic inflammations arise which may be divided, according to the mode of dissemination of the noxious matter, into lymphogenous and hæmatogenous. When the noxa—*e.g.*, a schizomycete—leaves behind no demonstrable change at the point where it entered the body so that the port of entry cannot be recognized, the inflammation is designated as cryptogenic. When the penetrated noxæ—*e.g.*, bacteria or virus—act mainly upon

the excretory organs, such as the kidneys, the liver, and the intestine, and are in fact passed out by them, the inflammation bears the character of an excretory inflammation.

Among the inflammations arising from external noxæ, those caused by circulatory disturbances—ischæmia, hemorrhages, stases, thromboses, etc.—are located at the points where the circulation is interfered with. In the formation of substances producing a chemical effect, which may arise both in the course of infections and also without these during functional disturbances in one or another organ, such as the intestinal canal, the liver, etc., the lymph and the blood are the carriers of the noxious agent, and accordingly we have here, too, lymphogenous and hæmatogenous toxic inflammations which likewise present the character of secretory inflammations in the organs in which these substances are discharged. Neuropathic inflammations may result from alterations or suspension of the tissue innervation which may produce circulatory disturbances, dragging, contusions, and other mechanical lesions, or else infection of the tissues. This will be the case especially when in consequence of sensory or motor paralysis the tissues are exposed to widely varying external influences, the latter being either unperceived or not evaded or removed on account of disability. Some authors are of the opinion that even disturbances of the vascular innervation may suffice to produce inflammatory symptoms directly.

In order to cause an inflammation, the influence of a noxa must not be too slight or too intense, for in the former case a tissue lesion —*e.g.*, a destruction of some isolated tissue cells—may indeed result, but no pathological exudation, while in the latter case the tissue is at once completely killed and an inflammation within the dead tissue is no longer possible. Slight injuries to the tissues will most readily assume the character of inflammatory diseases when capillaries and veins are situated within the confines of the lesion, and this will be the case particularly under hæmatogenous and lymphogenous influences, while ectogenous influences will frequently strike at first only non-vascular tissues. However, an inflammatory exudation may also be produced by these if the noxious agent or the injurious substance resulting from its action is carried into vascular regions through the lymph channels. Thus, for instance, a cauterization of the centre of the cornea may manifest its effect upon the marginal conjunctival vessels of the cornea, and as a rule mycotic colonies on the non-vascular portions of the cardiac valves sooner or later involve also the vascular tissue in the neighborhood.

In former centuries medical science applied the term "inflammation" only to morbid processes recognizable by the unaided eye. As

early as the beginning of the Christian era Celsus distinguished as the cardinal symptoms of inflammation redness (*rubor*), swelling (*tumor*), heat (*calor*), and pain (*dolor*), and up to the present day these cardinal symptoms, to which disturbance of tissue function (*functio læsa*) has been added, have maintained their importance. Our ideas of inflammation have, however, undergone some change in that we include among the inflammations also diseases of the tissues which lack a part or even all of these signs, or at least in which the signs are not recognizable or are no longer present at the time of the examination, so that the inflammatory nature of the process must be determined by other alterations which in part can be disclosed only by the microscope.

The reddening of an inflamed tissue is the result of fulness of blood which may present the character of a congestive or of a stasis hyperæmia. The swelling is caused partly by the greater distention of the blood-vessels, partly by the accumulation of exudates in the tissue, and in later stages also in part by the multiplication of tissue cells. The raised temperature of the inflamed tissue is due to an increased flow of blood through it. The pain and the functional disturbance depend partly upon the immediate action of the cause of the inflammation, partly upon the impeded circulation and nutrition, and partly also upon the exudation.

There has been much controversy as to which processes in the course of an inflammation are to be regarded as the most characteristic and indispensably necessary for the diagnosis, but thus far no decision has been reached; and the advances that have been made in our knowledge of pathological processes make it appear probable that we shall obtain unanimity in the views as to the nature of inflammation.

The perceptible rise of temperature of the inflamed part, which is due not to a local production of heat, but to an increased flow of blood through the affected region, is a symptom that manifests itself only in those parts, such as the external integument, which are exposed to cooling. The symptom is absent in inflammations of the tissue situated deep within the body, and persists even in the exterior parts only so long as the inflammation is associated with an increased local afflux of blood. It cannot be claimed, therefore, that it is an indispensable phenomenon of inflammation. The pain and the demonstrable disturbances of tissue function likewise presuppose definite forms and a severity of the inflammation exceeding a certain measure, for which reason they may be absent even in typical inflammations. Hence, starting with Celsus' symptoms of inflammation, the redness and swelling seem to be the most important manifestations, and indeed

the discussion as to the nature of inflammation up to the last decades has been mainly devoted to the question how the inflammatory hyperæmia and the formation of an exudation which cause the redness and swelling of the inflamed region are brought about and how these signs are to be interpreted.

The present views as to the nature of the inflammatory circulatory disturbances are based essentially upon investigations made by Cohnheim and Samuel in the sixties, which have since then been repeated and continued by numerous pathologists (Arnold, Thoma, Klemensiewicz). According to all investigations made within the last few decades, there can be no doubt that the pathological exudation from the vessels which characterizes inflammation is traceable to an alteration in the vessel walls; and this alteration is to be interpreted unquestionably as a degeneration, which in turn is nearly always one of the phenomena of a more or less extensive tissue degeneration. On the strength of this fact, which has been proved by various authors, we must consider the nature of inflammation as, first of all, a tissue degeneration associated with pathological exudations.

To this definition of inflammation the objection has been made that it does not apply invariably, inasmuch as a tissue degeneration cannot always be demonstrated. Concerning this criticism, however, it may be remarked that improved histological methods of examination have shown that the proof of degenerative tissue changes fails very rarely. Furthermore, it should be borne in mind that even in cases in which the tissue appears intact, and perhaps is so in fact, which is possible in hæmatogenous inflammations, an inflammatory exudation from the vessels is rendered possible only by an alteration of the vessel walls; and as the vessel walls certainly belong to the tissues a tissue degeneration must be present under such circumstances.

The circulatory disturbances and the formation of an exudation, which are partial phenomena of inflammation, may be followed in appropriate objects partly with the naked eye, partly with the microscope. In these investigations the preference is given to the ear of a white rabbit, in which the filling of the vessels and the onset of the inflammatory swelling are easily recognizable, to the web, the tongue, and the mesentery of a frog, to the wing membrane of a bat, and to the mesentery of a rabbit, all of which permit the direct observation of the circulation under the microscope. For the solution of such problems the cornea of various animals has also been used as a test object.

The mesentery of one of the animals named is put into an inflammatory state by the mere exposure and fixation to the stage, and in warm-blooded animals special arrangements are required lest the lesion of the tissue become too severe through drying and cooling so

that necrosis results instead of inflammation. Inflammations may be produced by mechanical or, better, by thermic or chemical lesions (cauterizations) in the tongue of the frog when turned outwards and fastened in an extended position, as well as in the external skin and in the cornea of a test animal. The first symptoms on the part of the vascular apparatus are usually characterized by a congestive hyperæmia with acceleration of the circulation, which is either an effect of nervous irritation or of stimulation of the vasodilators or of paralysis of the vasoconstrictors, or else is caused by a direct paralyzing or relaxing influence upon the respective arterial vessels and in part also upon the capillaries and their surroundings. It is a moot point to what extent this congestive hyperæmia represents a portion of the inflammatory process. Strictly speaking, it is merely a forerunner of the inflammatory disturbances of the circulation which may pass by without being followed by inflammatory exudation and need not always precede the latter, so that it does not form an indispensable phenomenon of inflammation. The congestive hyperæmia with accelerated current is sooner or later followed by a hyperæmia with retarded flow in the dilated channels, which is clearly recognizable particularly in the capillaries and veins, and is more pronounced in stretched membranes in which the several blood capillaries can be distinguished under the microscope. In the plasmic marginal zone of the blood current within the small veins, which zone under normal circulatory conditions is free from cells or contains leucocytes only temporarily, there appear in consequence of this tardy flow more or less numerous leucocytes that remain for some time in this zone and adhere to the vessel wall or else roll along it and then again cling to it or regain access to the axial blood current. Blood plates may also appear in the marginal zone, and if the retardation of the flow is more marked red blood corpuscles pass over into the marginal zone, and then the boundary between the axial red-blood current and the plasmic colorless marginal zone becomes obliterated. At this time, in the dilated capillaries the circulation of which varies in rapidity, red and white blood corpuscles mingle, and the number of the latter as compared with the former increases, owing to the adhesion occurring at the wall of the capillaries. Here, too, blood plates may become visible at this period.

The dilatation of the veins and capillaries and the retardation of the blood current find their explanation in an alteration of the vessel walls and of the tissue surrounding the capillaries, which tissue, owing to the thinness of the walls of the capillaries, bears a portion of the blood pressure in these. This alteration manifests itself in a certain weakness of the resistance to the blood pressure; parietal

changes which increase the friction act at the same time so as to slow the current, and this retardation in the veins is then followed by the escape of colorless and finally also of red corpuscles into the plasmic margins. The occurrence of blood plates is to be explained by the fact that in consequence of the circulatory disturbance plasmic constituents of decrepit red corpuscles in the form of blood plates separate from these, or that the blood corpuscles perish with the formation of these structures.

The above-described circulatory disturbances, which are sometimes more and sometimes less distinctly marked, are succeeded by the formation of the exudation, the escape of liquid and corpuscular constituents of the blood.

The liquid which passes from the capillaries and veins during inflammation is always more albuminous than the normal tissue lymph; but the amount of albumin varies according to the location and the intensity of the inflammation. Not rarely a deposition of fibrin takes place within the liquid exudation. Among the corpuscular elements that escape the colorless corpuscles predominate, though red blood corpuscles and blood plates may be associated with them. Of the colorless corpuscles transuded the most numerous are the multinuclear forms, which in normal human blood constitute about seventy per cent.

The escape of the colorless corpuscles is effected by amœboid movements of the cells adhering to the walls of the capillaries and small veins. In this act they protrude protoplasmic processes through the vessel walls, and finally the entire cell body, following the protoplasmic process, passes through the vessel wall. When red blood corpuscles likewise transude, the escape is effected, unless rupture of the vessels occurs, by their soft mass seemingly flowing through minute openings in the thin vessel wall.

The escape of the colorless corpuscles is an active process the result of amœboid movements of the cell protoplasm, and leucocytes may leave the blood current in capillaries without our being able to demonstrate an alteration in the vessel wall or to conclude from the concomitant phenomena that this has occurred (Thoma, v. Recklinghausen). The escape is, therefore, designated as an emigration. Still, when the escape is extensive—a feature characteristic of inflammation—there are changes in the vessel walls which favor the adhesion of the blood corpuscles and their emigration. On treating the vessels from inflammatory foci with silver nitrate these alterations can often be distinctly recognized (Arnold, Thoma, Engelmann, Löwit), the cement substance between the endothelial cells being irregularly distributed and widened in places. According to investi-

gations by Thoma, Binz, Appert, Pekelharing, Disselhorst, and others, the emigration of the leucocytes in the inflamed tissue may be arrested or at least diminished by irrigating the tissue—*e.g.*, the mesentery of the test animal—with a 1.5-per-cent. solution of table salt or with solutions of quinine, iodoform, or salicylic acid; and this phenomenon may be explained by the fact that such substances partly inhibit the motility of the leucocytes and partly produce also a contraction of the vessels, hinder the adhesion of the leucocytes to the vessel wall, and diminish the permeability of the vessels. The authors who have conducted these experiments attribute the chief influence upon the emigration sometimes to one, sometimes to another of these factors.

When in an inflammation red blood corpuscles also escape, as these are incapable of spontaneous movement, the phenomenon can be looked upon only as one in which the corpuscles remain passive, and therefore it is called not an emigration, but a diapedesis. It results from the pressure existing in the vessels, and is favored by an increased permeability of the vessel walls. It can be demonstrated that they are expressed, particularly in cases in which leucocytes likewise pass out, and that the escape of the red blood corpuscles is facilitated by an alteration of the cement substance between the endothelial cells, which manifests itself as a widening, especially at the point of contact of the cells. Whether blood plates escape as such has not been observed under the microscope. Their presence, however, both within and without the vessels in inflamed tissue renders it probable that this may be the case.

The view that the occurrence of the inflammatory exudation from the blood-vessels is to be ascribed first of all to alterations in the vessel walls has been advocated by Rokitansky. Vogel, Emmert, and Paget thought that this may be due to an increased attraction of the blood by the tissues. Virchow (1854), however, considered the free exudate collected in the fissures between the tissue and rising to its surface to be the result of the mechanical pressure within the vessels, while he interpreted the portion taken up by the cells as a kind of nutritive "educt"—*i.e.*, as the product of an increased attraction of the blood constituents by the irritated tissues. Even now he is still of the opinion that the cloudy swelling of the cells occurring in inflammation is the consequence of an irritation of these cells.

The authors of the last decades in general have abandoned the hypothesis that there is an attraction of the blood by the tissues; but in a more restricted sense it has again found defenders, inasmuch as some writers assume that in the emigration of the leucocytes the so-

called chemotaxis plays an important part. We have learned from the investigations of Leber, Massart, Bordet, Gabritchewsky, Buchner, and others that leucocytes are attracted by many substances—by products of the vital activity of schizomycetes, bacterial proteids, glutein-casein, the gluten of wheat, glue, etc., in thin solution—in the sense that they migrate in the direction of the greater concentration of the respective solution. Accordingly it is possible that such an influence by dissolved substances may be exerted upon the leucocytes present in the capillaries, but this may be assumed only when the corpuscles have already adhered to the walls and are in the act of emigrating. A decisive part, however, in the emigration of the leucocytes can hardly be assigned to chemotaxis, and the emigration certainly can occur without its becoming active at all. On the other hand, it frequently has an influence upon the behavior of the leucocytes in the tissues outside the vessels. Thus, for instance, it may explain the fact that leucocytes accumulate in large numbers around foreign bodies or bacteria which have penetrated into a tissue.

When with an inflammatory exudation an alteration of the vessel walls exists—an assumption now perhaps universally recognized—another question needs to be answered, namely, whether in that case the vessel wall is to be looked upon solely as a filter that furnishes products of different composition according to its state and the pressure to which its contents are exposed. This view has found numerous advocates, and even now is held by many pathologists. Still it is questionable whether the capillary walls can be regarded as a simple filter or whether they are not rather endowed with the qualities of a secreting tissue. The several capillaries, although apparently equal in structure, produce a tissue lymph of very variable composition. The contained albumin of the fluid in the cerebral and spinal cavities amounts to only 0.14 per cent.; that of the transudation in the pleural cavity, to 2.25 per cent.; that of the pericardium, to 1.83 per cent.; that of the subcutaneous tissue, to 0.58 per cent. (Reuss). According to Heidenhain, crystalloid substances (urea, sugar, salts) introduced into the blood do not pass into the tissue juices by a simple process of diffusion, but are rapidly carried into the lymph by the aid of a propelling force exerted by the capillaries. Moreover, by means of certain substances—*e.g.*, peptone, decoctions of the muscles of crabs or of the bodies of leeches—it is possible to secure an enormous increase of the transudation of water from the blood into the lymph, a phenomenon that may be best explained by the assumption that the capillary walls represent a secretory organ whose specific activity is altered by the substances named. Accordingly we are forced to regard also the formation of the liquid exudate

in inflammation as a disturbance of the capillary secretion, which view does not exclude the fact that aside from the changes in the walls alterations of the blood pressure likewise play an important part.

The tissue changes forming a partial phenomenon of inflammation are, as stated above and expressed in the definition of inflammation, at first of a degenerative nature, and the alteration of the vessel wall previously referred to is a part of the same manifestation. Inflammation, however, does not present a special form of tissue degeneration; on the contrary, all forms of the latter may occur in the course of inflammatory processes—*i.e.*, cloudy swelling, hydropic and vacuolar degeneration, fatty and mucoid metamorphosis, hyaline and amyloid degeneration, direct and indirect necrosis, gangrene, etc. Some of these alterations are the direct result of the action of the cause of the inflammation, others are secondary phenomena dependent partly upon the circulatory disturbances produced by the inflammation, partly upon the changes in quantity and quality of the lymph acting upon the tissue.

The exudate effused into the tissue collects at first as an infiltration in the fissures of the tissue and may distend it considerably. Often, too, it comes as far as the free surface of the affected tissue, especially in mucous and serous membranes, whence it flows off or it collects in the respective body cavities. A portion of the exudate, however, may also be taken up by the constituents of the tissue itself. This is observed particularly in cells rich in protoplasm, which when swollen often exhibit a change in their structure, a coarse granulation, and not rarely also drops of fluid, so-called vacuoles. Moreover, the cells of the exudate, the leucocytes, may penetrate into the tissue cells and be taken up by them in case they are capable of motion, so that we find tissue cells containing leucocytes. Often, too, there may be in addition a disintegration and a solution of the elementary constituents of the cells and of the fundamental substance in the exuded liquid. If at the same time a fluid rich in leucocytes is formed, it is called pus, and the process is known as suppuration.

The fact that inflamed tissue contained besides the liquid exudate a more or less large quantity of cells was explained by Virchow and his pupils, before the emigration of leucocytes was known, by the theory that the cause of the inflammation acted as an irritant upon the tissue and then produced a hasty division in its cells. The observation reported by Cohnheim in 1867 concerning the emigration of leucocytes, which confirmed the statements made by Dutrochet in 1842 and by Waller in 1846, but since forgotten, showed that there was also another source of these cell masses. It was inevitable that differences of opinion should arise as to the origin of the cell masses

present in inflammatory foci, and since 1867 this question has aroused a lively discussion that has continued to the present day.

Cohnheim himself at the time ascribed the entire increase of cells in recent inflammatory foci to the emigration of cells from the blood-vessels, and his view has been approved by many authors. Cauterizations of the cornea in test animals, which were frequently made in order to decide this question, enabled us to recognize the fact that the cells collecting around the eschar of the cautery arrived at the point of their accumulation by migration and were derived ultimately from the blood-vessels, while in the fixed cells signs of degeneration appeared first, and only after a relatively long time reparatory processes, so that therefore in recent inflammatory foci an increase of the cellular contents by division of the preëxisting tissue cells could not be demonstrated.

Among the authors who energetically opposed Cohnheim's views, Stricker is to be named first of all. The latter did not deny the occurrence of an exudation and the emigration of colorless and red blood corpuscles, but regarded the tissue infiltration observed in inflammation rather as an alteration of the formed elements and not as the product of an exudation. The hardening and the subsequent purulent deliquescence of inflamed tissue were said by him to be due to the fact that the cellular network which intersects the tissue—*e.g.*, that of the cornea and of the bone substance—swells and then divides into small nucleated segments, while the fundamental substance becomes reduced. This phenomenon is according to Stricker one of growth. Pus is formed after the consumption of the ground substance by the division of the cellular network into nucleated and small non-nucleated segments. An emigration of leucocytes from the blood-vessels may take place at the same time, but does not appertain to the nature of the inflammation and may be lacking.

Views resembling those of Stricker, but not exactly agreeing with them, have also been advocated by Heitzmann. The circulatory disturbances leading to pathological exudations and to the emigration of leucocytes are regarded by him as phenomena forming part of the process and as carrying to the tissue an increased amount of nutrient material. For the rest the nature of an inflammation is constituted by peculiar tissue alterations, which always begin in the connective tissue and only secondarily extend to the epithelia, muscles, and nerves, and which in general are characterized by the fact that the tissues return to their early condition. According to Heitzmann's view, tissues are built up from living material and its derivatives, in which process living material (cells) is preserved in the centres of the

tissue units, while at their peripheries the material is infiltrated with basis substance. In the inflammatory process the alterations are based upon a solution of the basis substance in the first instance, and upon an increased production of their like by the living material secondarily. When this takes place, not only the "cells" grow, but everything capable of life, hence also the portion of the living material enclosed in the basis substance. The inflammatory irritation and the added surplus of nutrient material frequently manifest their effect most prominently in the youngest portion of the tissue unit—*i.e.*, in the nucleated protoplasmic body usually called cell, so that it divides. The living material inclosed in the basis substance reacts to the altered afflux of liquid as a rule by solution of the basis substance. Then follow a rejuvenation of the material and its grouping around a certain number of centres, each of which encloses a nucleus. When the newly formed elements remain joined together, then there occurs a new formation of tissue, generally of connective tissue. When, however, the union of the living material is interrupted at many points and the connecting bridges between the several masses break, so that they float in a liquid basis substance, then the result is a formation of pus.

When more nutrition is supplied to the epithelial and endothelial cells by the inflammatory exudate, the living material increases, the elements become granulated and undergo cloudy swelling. If then the surrounding envelope of the several elements does not liquefy, there ensues an endogenous new formation of minute corpuscles which at first constitute coarse granules, then coalesce into homogeneous lumps, and finally become nucleated plastids. On the other hand, when the cement substance liquefies early, a number of elements melt into larger masses of bioplasm with nuclei which lead to the production of inflammatory corpuscles. In plastic inflammation the newly formed medullary inflammatory corpuscles remain joined together and lead to the new formation of connective tissue. But in purulent inflammation the union between the medullary elements resulting from the epithelia and endothelia is severed, and the medullary plastids, then called pus corpuscles, are set free by active emigration or by contraction of the bioplasm of the parent corpuscle.

The views of Stricker and Heitzmann regarding the nature of inflammation have in general met with little approval. They have their origin in notions about the structure of the tissues which agree in no way with those derived from the histological and developmental investigations made in recent years. Moreover, the description of the tissue alterations in inflammation is not exact, and is based upon methods whose insufficiency has long since been proven by thorough

and reliable procedures. These views, therefore, were regarded by most pathologists as controverted, until Grawitz in 1889 again advanced similar opinions and attempted to modify the notions prevailing as to the nature of the vital processes occurring in inflammation or to bring them back to a position resembling that advocated by Stricker and Heitzmann.

According to Grawitz, pus is liquefied connective tissue, "as taught in cellular pathology, though, of course, in a sense not hitherto imagined by anybody." "A fruitful and in some chronic inflammations perhaps the only source of cell formation is the intercellular substance." The emigration of leucocytes is an altogether incidental process, and there may be purulent disintegration of the connective tissue without any noteworthy participation of leucocytes. Thus far we have become acquainted with hardly more than five to ten per cent. of the connective-tissue cells. About ninety-five per cent. are in a condition inaccessible to our nuclear staining methods, and which, therefore, should be designated as a "slumbering condition." In the development of the tissues, the embryonal cells of the connective tissue are first largely changed directly into fibres. "Another portion of the embryonal cells falls into a slumbering condition without the formation of a single fibre, but rather so that the cells first form a plasmic channel; that is, a nucleated capillary tube whose wall gradually becomes also non-nucleated, nothing remaining finally recognizable but a small fissure as in quiescent tendinous tissue. A third portion of the cells passes within the fissures into the slumbering condition, while only in the larger permanent plasmic canals this third group continues always stainable; these are the fixed connective-tissue cells, thus far the only ones known."

In inflammation not only the fixed connective-tissue corpuscles come into action, but also the slumbering cells become mobile, first those within the fissures, then those about the fissures or plasmic channels, and lastly those enclosed in the fibres; they furnish a numerous small-cell infiltration, even before a single colorless blood corpuscle has emigrated or a single fixed cell has become mobile. The first thing to be noticed at the awakening of the slumbering cells is a small nucleus, at the poles of which some cell substance then appears, and by the further increase of this a cell results, and these new, "thus far unknown" cells are present partly within fissures, partly at the walls of the previously non-nucleated plasmic channels, and finally partly within the fibres.

Grawitz's description has not lacked some corroboration, but it soon encountered opposition, and, although not many authors have

expressed opinions about it, this was hardly because they agreed with him, but rather because they saw in Grawitz's slumbering cells the effect of a vivid imagination, as their existence was in no wise established by that author. And, in fact, it is clearly evident from the description and illustrations published by Grawitz and his pupils that in their investigations on inflammation they saw nothing that was not previously known, and that the novelty lies alone in the interpretation of the findings.

Even according to Grawitz's investigations there can be no doubt that the pathological exudation from the blood-vessels forms an integral, indispensable part of inflammation, and that the cells collecting in the inflamed regions are leucocytes, especially multinuclear forms, emigrated in the first place from the blood-vessels. The only point that remains doubtful is to what extent—aside from the more or less degenerated preëxisting tissue cells which stand out from the subjacent substance—leucocytes emigrated from other points, and tissue cells derived from division of preëxisting and sufficiently recognizable tissue cells in and near the inflammatory focus, may participate in the cell accumulation prevailing there.

In the first place, as regards the migratory cells discovered at the time by Recklinghausen in normal tissues, it is reasonable to assume that they occasionally also immigrate into inflamed regions; but, aside from lymphadenoid tissue formations, their number is too small to form an appreciable part in inflammatory cell accumulations. Of much greater importance is the participation of the multiplying fixed connective-tissue cells in the formation of the inflamed tissue. Since the improved histological methods of examination permit the positive recognition of the process of nuclear and cell division through its entire course, in which the alterations in the chromatophile substance of the cell nucleus clearly bring out the preparation for the division of the nucleus, histological investigations have been incessantly made with a view of establishing the progressive changes within inflamed tissue after traumatic lesions, thermic influences, cauterizations, and infections. We know, therefore, that about eight hours after the beginning of an inflammatory disturbance of nutrition there may be along with tissue degenerations a commencing tissue proliferation; that is to say, a formation of new cells by division of preëxisting fixed cells. We know, moreover, that the newly formed cells temporarily possess a certain motility and accordingly may change their position. Hence there can be no doubt that, aside from the preexisting, mostly degenerated cells detached from their normal combinations, newly formed cells are also admixed with those of the exudate. This admixture, however, commences at the earliest after

eight hours, is only slight in the first twenty-four hours, and does not reach any importance before the second or third day or later. Besides, their quantity varies according to the nature of the inflamed tissue. The covering epithelia and the ordinary connective-tissue cells are capable of a rapid and extensive proliferation, and the same is true of the endothelia and the connective-tissue cells of the blood-vessels and lymphatics. A slighter capacity for proliferation, but which may increase after the inflammation has existed for a longer time, appertains to the glandular epithelia, to the muscle cells, and to the glia cells. The cartilage cells and the cells of the heart muscle proliferate but little, and the bone cells and ganglion cells not at all.

The new cells resulting from division of the tissue cells can in general be very well distinguished from the exudate cells. Their finely granular protoplasm is most abundantly developed, the oval nucleus is clearly limited by a membrane, and its chromatophile substance is quite distinctly demarcated from the colorless caryoplasm; this is true not only of the descendants of epithelial cells, but also of the connective-tissue cells, which, owing to their resemblance to epithelial cells, are often called epithelioid cells. No confusion is possible with polymorphous nucleated or multinuclear leucocytes, whose nuclei and protoplasm are differently constituted and also react differently to stains, and the only subject for discussion is whether the proliferated tissue cells are not likewise changed into cells having the character of multinuclear leucocytes which are often described as pus corpuscles. Indeed, there is no lack of advocates of this view, but no facts are known that would justify such an assumption or would make this transition probable, so that the multinuclear leucocytes may positively be included among the exudate cells.

It is more difficult to distinguish the cells resulting from the proliferation of the tissue cells from the uninuclear leucocytes which may pass out from the blood-vessels in considerable quantities, especially in long-continued inflammations. Here, too, a differentiation may frequently be made by the size and constitution of the protoplasm and nucleus, and in part also by a special reaction of the latter to the Biondi stain; still, often enough we find inflamed tissue cells whose origin cannot at present be determined with accuracy.

The proliferation of the inflamed tissue or that situated in the vicinity of an inflamed focus constitutes an important process in the course of the inflammation, for it permits a restoration of the tissue which has become degenerated or lost through the inflammation. There was a time when the restoration of the lost tissue—*i.e.*, the healing of the defect by newly formed connective tissue (cicatrization)—was

ascribed to an activity of the exudate cells, at least to the uninuclear forms of these. This was at a time (in the seventies) when, owing to defective methods of examination, not enough was known about the capacity for proliferation of the tissue cells, and the power of migration had not yet been discovered. To-day most authors hold the view that new tissue can be produced only by old tissue in a state of proliferation, in which process each tissue forms nothing but its like or closely related tissue, so that epithelial cells produce only epithelium and connective-tissue cells only connective tissue. Still, even nowadays there are authors who do not recognize such a specific quality of the tissues and maintain that under certain circumstances epithelium, for instance, may also form connective tissue, but the experiences gained in pathology speak decidedly against such an occurrence in the developed organism.

Special tissue formations, such as epithelium, gland tissue, muscle, and glia tissue, can undoubtedly be produced only by corresponding tissue cells. As to leucocytes, only the ordinary connective tissue, which in destructive inflammations so very frequently replaces the lost specific tissues and forms the so-called cicatricial tissue, might come in question. With reference to this view the statement may be made that a formation of cicatricial tissue from exudate cells has not been demonstrated and is not probable; but, on the other hand, such a formation has not been positively excluded by reported investigations, so that the possibility of the occurrence must be conceded.

In recent years the question has been largely discussed whether the tissue proliferations represent an integral, necessary part of the inflammatory process. Neumann, Lubarsch, Ribbert, and others have pleaded in the affirmative. Neumann distinguishes in the course of an inflammation a primary effect produced directly by the cause of the inflammation, secondary disturbances representing the pathological consequences resulting from the primary effect, and a reaction; that is, those processes which again remove the primary effect and the secondary disturbances.

The various noxious influences cause tissue necrosis and thereby disturbances of the continuity of tissue; the succeeding processes—the exudation and the regeneration—are tending to the restoration of the interrupted continuity, and thus the regeneration forms an essential partial phenomenon of the inflammatory process.

It is an unmistakable fact that in some inflammations the proliferative processes play an important and characteristic part, and accordingly we speak also of inflammatory tissue proliferations, of proliferating or granulating or plastic inflammations. From this

alone, however, it does not follow that proliferative phenomena are absolutely essential in order to give a pathological process the character of an inflammation. In the first hours of an inflammation, when a profuse exudate is present, when redness, swelling, and pain already sufficiently establish the inflammatory nature of the process, no tissue proliferations exist, and in purulent and gangrenous inflammations which extend rapidly to neighboring regions signs of proliferation may be completely lacking even for a lengthy period. Moreover, it is likely that in very slight hæmatogenous inflammations, though vascular and ultimately also tissue degenerations may occur and be associated with pathological exudations, cell disintegration and subsequent phenomena of proliferation may remain absent. It is safe to say, therefore, that in order to characterize a process as an inflammation the existence of proliferative manifestations is not necessary. On the other hand, experience teaches that when the process is sufficiently prolonged, a proliferation follows the degenerative processes with very rare exceptions, and hence in the definition of inflammation this fact should be expressed, as has been done in the introduction.

The proliferative processes in the course of inflammations have in general a regenerative character and follow after the tissue degeneration. This does not mean, however, that regeneration and inflammatory tissue proliferations are identical conceptions. When after a loss of substance—for instance, after removal of the covering epithelium—this is restored simply by division of the neighboring cells, we have a regeneration to which no one will apply the character of an inflammatory proliferation. The inflammatory nature of the proliferation is manifested only when pathological exudations impart to the entire process a peculiar feature. What is called a formation of inflammatory granulations is proliferating tissue, germinal tissue, in which the neoplastic process is accompanied by pathological exudations and the proliferating tissue cells are mixed with exudate cells. When the pathological exudations diminish and disappear altogether, then the inflammation declines at the same time, and with the dissolution of the inflammatory infiltration the process may also assume more and more the character of a pure regeneration.

The healing processes that produce the conclusion and the termination of an inflammation consist essentially in this, that on the one hand the alteration of the vessel walls and with it the pathological exudations are arrested, and on the other hand the pathological exudates and dead tissues are removed and the losses of substance which have arisen in the course of the inflammation are replaced. The former factor presupposes that the originally active cause of the

inflammation is no longer present and that no new noxæ influence the vessel walls, when under the conditions of normal nutrition the restoration of the vessel walls is effected by the circulating blood. The removal of the exudate is brought about partly by its being passed outwards, partly by absorption and incorporation into the mass of the body fluids, the lymph channels being chiefly active in the removal, although the blood capillaries may take part in the absorption. Firm, coagulated exudates and necrotic tissue must be dissolved before they can be absorbed, they becoming either liquefied to a considerable extent or else gradually destroyed by living cells.

The restitution of the tissue degeneration, when the alterations are slight and not associated with losses of substance, may be effected by the changed tissue elements returning to the normal under the influence of the restored circulation. The healing of losses of tissue is possible only by new formation, and, as has been repeatedly stated above, earlier or later in the course of the inflammation proliferative processes occur which serve for the restoration of the lost tissue and may therefore be included among the healing processes. When the loss is replaced by tissue exactly like that previously present, the healing is perfect, so that the inflammation leaves behind absolutely no permanent change. When only connective tissue forms in place of the lost substance, while the specific tissue of the affected organ—glandular, muscular, cerebral tissue, etc.—is not at all or but imperfectly re-formed, then the healing is incomplete and terminates in the formation of a cicatrix. When connective tissue is formed extensively or in excess, the result may be fibrous sclerosis of an organ as well as agglutination of adjoining organs.

The course of an inflammation is sometimes brief, sometimes greatly prolonged, so that acute, subacute, and chronic inflammations are to be distinguished. An acute course ending in rapid recovery presupposes that the cause of the inflammation has acted for a short time only and caused no serious tissue lesions. More prolonged inflammations result either when a noxa acting but once and for a brief period leaves behind grave tissue lesions (extensive comminutions, tissue necroses, large burns, massive exudates) the healing of which consumes much time, or when a noxa acts repeatedly (continued inhalation of dust, prolonged friction or contamination of the skin, protracted excretion of toxic substances by the kidneys), or else when a noxious agent remains within the body and perhaps even increases in it. In the latter case, which occurs particularly in infections whose parasites do not perish in the body, but multiply at least here and there and advance locally farther into the tissue or are carried away in the lymph and blood current, the inflammation not only

becomes chronic, but may even manifest a progressive character and be distinguished by metastases.

When an organ is in a state of inflammation, it is customary to express this fact by appending the ending "itis" to the Greek or sometimes to the Latin name of the organ. Thus the terms pleuritis, peritonitis, pericarditis, myocarditis, endocarditis, metritis, nephritis, hepatitis, pharyngitis, encephalitis, meningitis, conjunctivitis, tonsillitis, etc., are used in this sense. When the intention is to imply that the serous covering or the surroundings of an organ are inflamed, we add to the corresponding word the prefix "peri" or "para"; thus, perimetritis, parametritis, perihepatitis, perinephritis, perityphlitis, etc. For some forms of inflammation special names are in use; thus an inflammation of the lung is usually called pneumonia.

The Various Forms of Inflammation.

In order to gain a better general view of the inflammatory processes which occur in different forms, certain types may be set apart in which sometimes the site of the inflammation, sometimes the quantity and quality of the exudates, sometimes the behavior of the tissues present the characteristic features.

In the first place we may distinguish superficial and deep-seated inflammations, the former being represented chiefly by inflammation of the skin, of the mucous membranes, and of the serous coverings; while the latter are located particularly in the glands, the nervous system, the muscular apparatus, the osseous system, the subcutaneous, submucous, and subserous tissues.

It is a characteristic feature of superficial inflammations that the exudate comes to the surface and also that the degenerative tissue changes run their course mainly in the superficial cell layers. Continuous liquid excretions from mucous membranes, which are mixed with secretory and degenerative products of the epithelia or with entire epithelial cells, and emigrated leucocytes or pus corpuscles form the foundation of inflammations of the mucous membranes designated as catarrhs. When the inflammatory secretion from a canal invested with mucous membrane cannot escape by reason of special conditions, for instance in consequence of partial occlusion, exudates accumulate and cause dilatation of the canal. This is observed most frequently in the Fallopian tubes after occlusion of the abdominal ostium and in the uterus after stenosis of the os. Processes of coagulation in superficial exudates give rise to more or less dark coherent membranes which if fibrinous are called croupous membranes.

Inflammations of the superficial layers of the external integument

which are of a certain intensity and duration often lead either to exfoliation or desquamation of the epithelium or to vesication in which the corneous layer of the epidermis is elevated by an exudate, while at the same time the deeper, not cornified layers of the epithelium in the region of the blister become partly or wholly dissolved and liquefied. Perforation of the corneous layer by persistent exudates or oozing of the exudate through less coherent corneous layers cause weeping inflammations of the skin which may be likened to catarrh of the mucous membranes. Drying of the exudate that has risen to the surface or of blisters filled with exudate gives rise to the formation of crusts or scabs.

Superficial inflammations of the lung are characterized by filling of the pulmonary alveoli and bronchioles with exudate whose quality may vary according to the nature of the inflammation. In superficial inflammations of the serous membranes the exudate collects in the corresponding body cavities. A separation of fibrin usually leads to a deposition of tough, adherent fibrinous membranes upon the inflamed serosa. In most of the superficial inflammations, therefore, a pathological exudation on the surface forms a characteristic phenomenon, and the microscope shows that this exudation is associated with degenerative alterations of the epithelial covering, which not rarely, especially in fibrinous or croupous inflammations, causes complete destruction of the epithelial covering over large regions. Of course, under these circumstances the subepithelial tissue—*i.e.*, the connective tissue of the skin, of the mucous membrane, of the serosa, and of the lung—does not remain unchanged; for it is the support of the blood-vessels that exist at the site of the hyperæmia and exudation, and accordingly a superficial exudation presupposes an inflammation of the respective connective-tissue parenchyma.

In inflammation of connective-tissue parenchyma the exudate is situated chiefly in the interspaces of that tissue and in the lymphatics, though the connective-tissue cells may also imbibe a portion of the exudate and then become swollen and permeated by vacuoles—*i.e.*, drops of liquid. Specially receptive are the loosely constructed subarachnoid and pial tissues, and submucous, subcutaneous, and subserous formations, among which the latter reach a considerable thickness particularly in the lesser pelvis and in the mediastinum.

In inflammation of the glands it is sometimes the degenerative processes in the glandular parenchyma, sometimes the accumulated exudates in the sustentacular tissue that occupy the foreground, and this has led some to distinguish parenchymatous and interstitial inflammations. As a matter of fact, cases are met with—for instance, in the liver—in which the degenerative changes in the gland cells at-

tain uncommonly high degrees and cause destruction of the gland tissue, while the masses of exudate in the interstices of the tissues are relatively insignificant. On the other hand, the cell accumulations in the sustentacular tissue may reach considerable dimensions without any marked degeneration being manifest in the glandular parenchyma. Nevertheless, interstitial and parenchymatous gland inflammations cannot be strictly separated from each other, but combine in various ways and also pass one into the other in the course of the disease. We may, therefore, often be in doubt—for instance, in inflammations of the kidney—whether to call the disease a parenchymatous or an interstitial inflammation, and the choice of the term frequently depends largely upon the fact whether the treatment of the microscopic preparation has rendered the degenerative changes of the epithelium or the inflammatory exudates more conspicuous.

When exudates or even desquamated and degenerated epithelia are situated at the same time in the capsular space of the glomeruli and in the tubular system of the kidney, the disease may also be included among the superficial inflammations, and accordingly we may speak of catarrhal and croupous inflammation of the kidney or nephritis.

In inflammations of the muscular tissue we may distinguish, according to the seat of the tissue proliferations, parenchymatous and interstitial forms, as in the case of glands, and this distinction can even be made more strictly than with the latter. There are noxæ that cause preëminently degenerative changes of the contractile elements and relatively slight exudation, while in other diseases—for instance, those caused by pus cocci in infections—the accumulated exudate, especially the infiltration of the connective tissue with pus corpuscles, predominates in the microscopic picture, at least for a considerable time.

Finally, inflammations of the central nervous system and of the peripheral nerves may also be divided into parenchymatous and interstitial forms, since sometimes the degeneration and the disintegration of the nerve cells and fibres predominate, sometimes again cell accumulations in the perivascular sheaths of the blood-vessels of the brain and spinal cord, or in the endoneurium, perineurium, and epineurium of the peripheral nerves, constitute the essential findings in the histological examination. Here, too, however, it should be noted that the two conditions may be combined or that the appearances may change in the course of the disease, the degeneration of the nervous elements inducing exudations and proliferations within the sustentacular apparatus, while on the other hand the interstitial changes in turn may have a degenerative effect upon the nervous tissues.

The composition of the exudates depends, above all, upon the nature of the noxious influence, and accordingly presents not only a landmark for the differentiation of various forms of inflammation, but is at the same time a criterion for estimating the gravity of the inflammation.

Serous exudations, representing a clear or slightly turbid liquid which resembles the normal tissue lymph but contains a greater amount of albumin and more cells, are indications of a relatively slight inflammation that may pass rapidly or persist longer. Such an inflammation, unless special epithelial alterations are superadded, presents the character of a serous catarrh in mucous membranes, while in the skin the implication of the epithelium leads to œdematous swelling of the epithelium and vesication, in the lung to filling of the alveoli with fluid—inflammatory pulmonary œdema. In inflammation of the serous membranes the affected body cavities become the seat of more or less considerable accumulations of fluid. Within the varying tissue parenchyma the interspaces first receive the fluid, so that the tissue increases in volume and grows more succulent, the condition resulting being known as inflammatory œdema.

In serous inflammations the tissue suffers relatively little, but there is no lack of degenerative alterations, especially fatty changes and swelling of the cells. In mucous and serous membranes and in the lung there is at the same time a desquamation of the epithelium; in the skin more or less epithelia are detached at the site of the blister. In the connective tissue the swelling cells are at least loosened from the subjacent structures and some of them may perish.

Exudations containing many cells (leucocytes) cause at first a small-cell infiltration of the inflamed tissue. When a whitish fluid rendered turbid by the admixture of numerous leucocytes or pus corpuscles reaches the surface of a mucous membrane, the appearance presented is that of a purulent catarrh; under the corneous layer of the skin, in the region of the melting or liquefied epithelium, it causes the formation of a pustule or of an epithelial abscess.

Direct infiltration of a tissue with pus corpuscles, which impart to it a whitish or yellowish-white tinge, is known as purulent infiltration, and when much fluid is present at the same time as purulent œdema. When in the locality of the purulent œdema or of the purulent infiltration there are liquefaction and deliquescence of the tissue with the resulting formation of a cavity filled with whitish fluid, the condition is called abscess (connective-tissue abscess, gland abscess, lung abscess, muscle abscess, brain abscess, etc.), and the process causing the cavity formation, suppuration. Inflammations in which the purulent infiltration and the suppuration spread over

larger regions—*e.g.*, pea-sized areas in the subcutaneous or submucous tissue—are designated phlegmons, pus collections in the body cavities are called empyemas, in the tubes pyosalpinx, in the uterus pyometra.

Suppuration, purulent disintegration, and abscess formation are to be regarded as grave forms of inflammation which are usually caused by bacteria, especially the so-called pus cocci, though the colonization of the respective bacteria does not always produce suppuration, and other noxæ likewise—*e.g.*, chemically active substances such as oil of turpentine, petroleum, mercury, five to ten per cent. solutions of silver nitrate, diluted croton oil, and different sterilized bacterial cultures—may set up suppuration. The suppurations caused by chemical substances as compared to infectious suppurations are peculiar in that they heal more quickly, do not spread in the tissues, give rise to no metastases, and in that their products have no virulent effect when inoculated.

Fibrinous or croupous inflammations are characterized by a deposition of fibrin within the exudate and occur most frequently at the surface of mucous and serous membranes and in the lungs. In slight and recent fibrinous inflammations the normally smooth and glossy surface of the serous membranes—the pericardium, the pleura, the peritoneum, the tunica vaginalis testis—appears opaque and rough. When the process is more pronounced, the surface is covered with whitish or yellowish felted, or perhaps villous, tough membranes which are either firmly adherent or may be easily detached. When the fluid present is scanty, there may often be adhesions of opposite surfaces of the affected serosa.

On mucous membranes there are formed circumscribed or more extensive whitish, yellowish, or, owing to impurities, dirty colored more or less firmly adherent membranous deposits seated on a reddened base. They are observed most frequently on the mucous membrane of the palate, pharynx, and respiratory tract, but occur also on other mucous membranes. In the lungs fibrinous or croupous inflammation causes a filling of the alveoli and bronchioles with firm gray, yellowish, red, or grayish-red masses, which adhere to the walls and usually displace all the air so that the lung undergoes a hardening known as hepatization.

Fibrinous superficial inflammations are to be included among the grave forms and are as a rule due to infection. In the pharynx and the respiratory tract the most frequent causes are diphtheria bacilli and streptococci; in the lungs and the serous membranes, pneumococci and streptococci; but croupous inflammations may also be produced by other bacteria (tubercle bacilli) and by irritating chemicals.

At the time when the croupous membrane forms the epithelium has usually already perished or is present only in degenerated or necrotic remnants upon and in the fibrinous deposits. This statement applies not only to the single epithelial layer of the serous membranes and the lung, but also to the stratified epithelium of the pharynx, palate, and respiratory tract. Croupous membranes, therefore, are for the most part located immediately upon the connective tissue, though here and there they may cover the remaining epithelium.

On mucous membranes the fibrin mostly forms threads having a reticulated arrangement and adhering to the surface of the connective tissue or penetrating into it, and thus favoring the attachment of the false membrane, especially at the points where the surface is irregular and devoid of a dense limiting membrane—*e.g.*, in the pharynx, at the epiglottis, and on the vocal cords—while the smooth investment of the connective tissue with a limiting membrane hinders the adhesion, as in the trachea and the bronchi. The fibrinous network encloses more or fewer leucocytes and in recent affections also necrotic epithelium. Not rarely the false membranes are stratified, new exudates being deposited at intervals. The most superficial, oldest layer may therefore contain necrotic epithelia, while the lower, more recent strata may enclose only pus corpuscles.

The connective tissue of the mucous membranes covered with fibrin is always more or less markedly altered, being hyperæmic, infiltrated with liquid exudate and leucocytes, here and there also often penetrated by aberrant threads of fibrin. Frequently reticulated or radiating masses and bunches of fibrin threads and rods may be present in the hyperæmic blood-vessels, in which case, of course, it is at times hard to decide how much of the fibrin may have been deposited during life and how much after death. At all events, not only the exudate but also the blood plasma shows a tendency to the deposition of fibrin. Much fibrin ferment, therefore, must form in such foci, and the conditions for the coagulation must be furnished both by the exudate and by the blood itself. Degeneration and disintegration of red and colorless blood corpuscles are apt to give rise to ferment as well as to fibrinogen substance.

Fibrin occurs in a similar thready form as it presents on mucous membranes also in croupous pulmonary inflammations and adheres to the walls of the alveoli, since these likewise are the seat of an inflammatory hyperæmia and of a cellular, serous, and often even of a fibrinous infiltration. Within the meshes of the fibrinous network of the alveoli are more or less numerous leucocytes and degenerated exfoliated epithelia, frequently also red corpuscles.

The deposits of fibrin upon serous membranes are often granular

or flaky or trabeculated or gathered in irregular, dense, smeary masses that include only few cells; still, especially on the peritoneum, fine fibrillated layers of fibrin containing many pus corpuscles are also met with. The close adhesion of homogeneous-looking trabeculæ of fibrin to the subjacent connective tissue led Neumann, Grawitz, Delbanco, and others to assume that in acute fibrinous inflammations of the serous membranes there is a fibrinoid degeneration of the connective tissue; that is to say, a hyaline change of the superficial connective-tissue layers which at the same time increase in volume. According to Neumann, it is this fibrinoid metamorphosis that causes the opacity of the serous membranes in inflammation and the formation of the adherent false membranes. However, appropriate methods of examination demonstrate that these hyaline trabeculæ are nothing but the exudated fibrin which in recent inflammations is resting immediately upon the connective tissue. In inflammations of several days' standing these fibrinous trabeculæ may in part already be infiltrated with germinal tissue sprouting from the connective tissue and thus, as it were, be incorporated into the serous membrane. The connective tissue of serous membranes in fibrinous inflammations is, according to the intensity of the process, sometimes hyperæmic and infiltrated with liquid and cellular exudate, sometimes in a state of active proliferation, so that the multiplication of the cells is largely attributable to a division of the tissue cells. Occasionally exudated fibrin in the shape of filiform masses may also be demonstrated in the connective tissue as well as in the blood-vessels and lymphatics, though as a rule not so plentifully as in inflamed mucous membranes. Finally it may happen that the connective-tissue trabeculæ, owing to infiltration with exudate, may acquire a swollen homogeneous appearance, but with appropriate treatment such formations can be clearly distinguished from hyaline fibrinous trabeculæ, nor do they constitute a part of the superficial fibrinous membranes.

In deep-seated inflammations, in submucous and subcutaneous tissues, in lymph and other glands, in muscles, and in the nervous system, deposits of fibrin may likewise occur, though rarely in such masses as to attract attention on histological examination. These thready deposits of fibrin are most frequent in inflamed lymph glands and in subcutaneous and submucous tissues, so that the process here may be designated as a fibrinous and croupous inflammation. The threads of fibrin usually include leucocytes and sometimes also red blood corpuscles.

In inflammation of the kidneys we may very often meet with deposits from the albuminous urine in the shape of hyaline coagulated

masses in the capsular space of the glomeruli and in the urinary canaliculi. Under appropriate treatment threads of fibrin may also now and then be demonstrated.

Hemorrhagic inflammations—that is to say, such as are characterized by the diapedesis of numerous red blood corpuscles, and therefore by a sanguineous nature of the exudate—presuppose for their origin a more marked alteration of the vessel walls or more pronounced circulatory disturbances. In the former direction is the activity of some infections (hemorrhagic septicæmia, smallpox) and of intoxications (snake poison, phosphorus), in the latter of intense stases. Moreover, it should be noted that the escape of red blood corpuscles occurs more readily in some organs than in others; for instance, it happens with special facility in the lung.

In superficial inflammations the blood, becoming mixed with the exudate, may rise to the surface, as in the lung or in the intestine. In the skin hemorrhagic blebs may form. Otherwise both in superficial and in more deeply seated inflammations the tissue is more or less profusely infiltrated with red blood corpuscles and may thereby acquire a red or blackish-red appearance.

Serous, purulent, fibrinous, and hemorrhagic exudates may combine in manifold ways. The most frequent are serofibrinous inflammations of the serous membranes, seropurulent inflammations of the mucous membranes and of the subcutaneous and submucous connective tissue (purulent œdema), pyofibrinous inflammation of the serous membranes, particularly of the peritoneum, pyofibrinous and sanguinofibrinous inflammations of the lungs. These mixed forms occur either from the start as such or a mixed form develops from an originally simple variety. A fibrinous inflammation of a serous membrane, for instance, becomes serofibrinous by a greater accumulation of liquid, pyofibrinous by a profuse escape of pus corpuscles, in which case the fibrinous membranes become whitish and friable. Hemorrhage from newly formed vessels in protracted fibrinous pleuritis or pericarditis may produce a sanguinofibrinous inflammation.

The tissue degenerations forming a portion of the inflammatory process are due either to the originally active noxa or to the circulatory and nutritive disturbances ensuing in consequence of the vessel-wall alterations and the accumulation of the exudate. The variety and nature of such degenerations, therefore, furnish some criteria for estimating the gravity of the primary tissue lesions or of the subsequent nutritive disturbances.

In inflammations of membranes covered with epithelium an important part is played by the swelling, disintegration, and solution, especially with the formation of vacuoles, and also desquamation of

the epithelium. Inflammatory vesication of the skin is always associated with processes of swelling and liquefaction in the epithelium. In serous membranes even slight inflammations cause swelling, fatty degeneration, and desquamation of the epithelium. In mucous membranes there is frequently added to these processes a mucous transformation of the epithelium, and often the production of mucus completely predominates in the manifestation of the inflammation, so that they are designated as mucous catarrhs. The admixture of numerous pus corpuscles which renders the glairy mucus turbid gives rise to a mucopurulent catarrh.

The connective-tissue cells, gland cells, muscle cells, nerve cells, lymph cells, etc., likewise undergo various degenerative changes, often advancing to complete destruction, in inflammations progessing in the depth of the tissues. In largely cellular organs, such as the liver, kidneys, heart, muscles, and brain, these degenerations can frequently be recognized with the naked eye by changes in the color and consistence of the organ. A dull appearance of the cut surface, gray, yellow, and white colorations point to albuminous and fatty degeneration of the tissue elements. Softening and liquefaction indicate disintegration and solution. These forms of inflammation may be characterized by the term degenerative and colliquative inflammations, and we may speak of inflammatory tissue degeneration, of softening and of liquefaction of the tissues. The above-mentioned tissue suppuration is nothing but a liquefaction and solution of the cells and of the basis substance of the dead tissue combined with the accumulation of fluid containing pus corpuscles; the process causing in the depth of the tissue an abscess, at the surface an ulcer, and by perforation of deep-seated foci towards the surface a fistulous tract.

When at the onset or in the further course there are formed larger, macroscopically visible tissue necroses which persist as such for some length of time, and are cast off or liquefied only after a certain period, we may designate the inflammation as necrosing. Superficial tissue necroses resulting from caustic chemicals or from heat or cold are often called eschars. Inflammations of mucous membranes leading to necroses are partly designated as diphtheria and are characterized by the formation of superficially visible gray and white or discolored spots. On mucous membranes provided with stratified pavement epithelium this discoloration may be due solely to epithelial necrosis, so that we may speak of an epithelial or superficial diphtheria. Thus, for instance, the formation of the true croup membrane on the pharynx in diphtheria may be preceded by such an epithelial necrosis. Usually, however, we are confronted with a deep-seated necrosis affecting also the connective tissue of the mucosa and

in pharyngeal inflammations implicating especially the lymphadenoid tissue. Necrosing inflammations occur in the upper digestive tract, both in ectogenous and in hæmatogenous infections and intoxications, chiefly in consequence of the ingestion of caustic fluids, but also as a result of infection with diphtheria bacilli and streptococci which, aside from croup, not rarely cause deep necroses, especially on the tonsils. In the lower part of the digestive tract extensive necroses of the mucosa occur, particularly in dysentery and in the later stage of cholera, and also in septic infections and sublimate poisoning. Infection with typhoid bacilli causes necrosing inflammations in the region of the lymphadenoid apparatus of the intestine and in the mesenteric glands.

In all of the last-named inflammations it is the tissue infiltrated with exudate, with leucocytes, not rarely also with red blood corpuscles and with fibrin, that undergoes necrosis and then first forms an eschar which later on is cast off by liquefactive processes at the border between the living and dead substance, leaving behind an ulcer. But if the latter is deep seated the eschar remains in the body, is gradually absorbed, and is replaced by connective tissue or becomes encapsulated.

Inflammatory tissue necroses possessing the character of gangrene arise in two ways: either gangrene-producing microorganisms penetrate into some tissue from the start, or else necrotic or inflamed tissues are secondarily infected with microbes that cause putrid, stinking decompositions of albuminous bodies. An especially frequent location of such inflammations, in which the tissue is changed into a foul-smelling, discolored, ragged mass and finally dissolves, is the lung, where both hæmatogenous and ectogenous or bronchogenous infections may take this course. Besides, infections of the skin, of the subcutaneous tissue, of the uterus and its appendages, peritoneal inflammations springing from the intestine, and inflammations of the efferent urinary passages not rarely present a gangrenous character, often combined with purulent inflammation. Occasionally putrid inflammations give rise to the development of gas.

Necrosing inflammations in the form of cheesy necrosis or caseation occur almost without exception in the course of tuberculosis. The dead tissue resembles sometimes hard cheese, sometimes cream cheese, and the peculiar cheesy masses result from necrotic processes within newly formed cellular, at times also fibrin-containing nodules, the cells perishing, and partly hyaline, partly granular products are formed.

Inflammations whose most prominent feature is tissue proliferation, and which accordingly are designated as proliferating, or granu-

lating, or plastic inflammations, represent usually only later stages of various forms of traumatic, thermic, toxic, and infectious inflammations in which the tissue proliferation must be regarded as a healing process and is likely to terminate the lesion. Still, inflammations occur, especially infectious forms (tuberculosis, lepra, actinomycosis), in which the tissue proliferation constitutes a marked partial phenomenon during the entire course, so that the above-mentioned designations are fully justified.

Inflammatory New Formation of Tissue.

The new formations of tissue occurring in the course of inflammations present to a great extent the character of regenerative processes, but often there may also be an excessive tissue formation which may give rise partly to pathological increase of volume and induration of the affected tissue, partly to pathological adhesions. The cause of the regeneration is based on the loss of tissue; hypertrophies, indurations, and adhesions of the tissues which presuppose a prolonged duration of the pathological proliferation are the result partly of the repeated action of noxæ from without or from within the body, partly of the residues of acute inflammation in the shape of existing necrotic tissue or large quantities of exudate difficult of removal. To some extent, too, they are the product of a special influence exerted by the exciting cause of the inflammation—*i.e.*, vegetable and rarely also animal parasites that remain in the tissues, grow or multiply there, and often penetrate into the neighboring regions or spread through the lymphatics and blood-vessels. Thus, for instance, an echinococcus cyst causes by its growth a continuous proliferation of the surrounding tissue; the itch mite, multiplying, keeps up a permanent inflammation of the skin; tubercle bacilli, increasing in numbers within the body, produce ever new granulations leading partly to connective-tissue hypertrophy and induration, partly to the formation of cheesy foci.

The reparative new formation of tissue, ending in the replacement of the inflammatory tissue degeneration and the *restitutio ad integrum*, is effected by mitotic division of the intact tissue cells in the vicinity of the defect and by the development of the germinal tissue resulting therefrom. In a mucous membrane which has partly lost its epithelium by mucous transformation and desquamation the epithelium is restored by this proliferation, and the same is true for serous membranes. In the lung the lost epithelial covering of the alveoli is replaced, while at the same time the exudate in the latter is again absorbed or expectorated. The epithelial defect in the re-

gion of blebs and pustules of the skin is repaired by proliferation of the neighboring epithelia, and beneath the drying vesicle or pustule a new corneous layer is formed by processes of cornification, and thus the degenerated tissue is gradually detached from the remaining skin.

Defects in the connective tissue of the cutis and of the subcutaneous tissue, of the mucosa and of the submucous tissue, of the serous membranes, of the fibres of tendons, etc., are filled up by connective tissue which, while it differs more or less in its structure from the normal tissue and is often functionally inactive, suffices for the restoration of the interrupted continuity.

When periosteum and bone marrow proliferate in the course of inflammations, they produce partly new periosteum and bone marrow, partly cicatricial tissue, partly also cartilage and bone. Perichondrium usually produces connective tissue and bone, rarely cartilage. Defects in cartilage are generally filled up by proliferation of the neighboring perichondrium, bone marrow, or synovial membrane, which produces connective tissue, or medullary tissue, or else bone. Only under special conditions, in prolonged slight inflammatory states of irritation, does the cartilage proliferate and produce cartilage or bone. Lost gland cells, renal epithelia, or liver cells may be replaced, if the glandular structure is preserved, by proliferative processes in the remaining gland cells. Regeneration fails, however, whenever the structure of the organ is more markedly altered; that is to say, whenever the glands have been entirely lost over larger regions or the continuity of the tissue has been interrupted by traumata or by necrosing or similar inflammations. In such a case only connective tissue is produced at the point of the lesion, while the gland tissue is not at all restored, or at least is so merely in rudimentary forms that are functionally of no value. Functionating gland tissue is re-formed most frequently in salivary glands. In the liver there are formed at the point of the lesion new biliary passages in the proliferating connective tissue, but they are of no use for the function of the liver and consist chiefly of solid cell cords. In the kidneys the regenerative gland production is even less in degree and is often altogether absent. In like manner the local gland regeneration remains very slight or fails to occur in the thyroid gland and in the genital glands.

In glands whose function is essential to the preservation of life and whose development and activity are in definite relations to the demands made upon them, such as the liver and the kidneys, compensation may be made for the defective local reproduction of the lost tissue by a compensatory functional hypertrophy of the intact gland tissue, in the sense that in the liver the glandular lobules and in the

kidney the glomeruli and the urinary canaliculi enlarge by augmentation in volume and by numerical increase of the gland cells.

Inflammatory losses of tissue in the central nervous system cause proliferations partly of the glia tissue, partly of the connective tissue, and these may combine in different ways or one alone may occur. The connective-tissue proliferation starts partly from the pia, partly from the blood-vessels and their pial sheaths, while the glia new formation springs from the glia cells.

In inflammations of peripheral nerves the connective tissue first proliferates and produces new connective tissue. When nerve fibres are destroyed, the axis cylinder that has remained in connection with the ganglion cell appertaining to it is capable of outgrowth. Hence the inflamed nerve region, or the connective tissue newly formed from the nervous connective tissue, may be perforated by axis cylinders which subsequently are surrounded with a medullary sheath.

In all proliferating inflammations of muscle the connective-tissue proliferation occurs first and produces cicatricial tissue. In the further course new muscle fibres may also form and pass through the cicatricial tissue. This takes place most profusely in the striated muscles of the body, but even here the local regeneration does not always suffice to compensate the functional disturbance. The lack of power of the muscle may then be made up by functional hypertrophy of the intact fibres. A new formation of smooth muscle fibres occurs only to a slight extent. The new formation of heart-muscle cells has not been demonstrated, but under increased demands the muscle cells undergo functional hypertrophy.

The walls of inflamed large blood-vessels produce in the main new connective tissue in which later on elastic fibres may develop.

As may be gathered from what has been stated, aside from covering epithelium, the production of connective tissue, especially of the ordinary variety, occupies the foreground in inflammations and often forms the only new tissue present. This connective tissue always develops by proliferation of the preëxisting connective tissue of the affected organ, and when the tissue production is considerable is associated with the formation of new blood-vessels. In open wounds or at the margin and the bottom of ulcers, around abscesses, etc., this germinal tissue forms soft masses of a red color due to an ample blood supply and of a somewhat bossy appearance, usually known as granulations or granulation tissue. The complete correspondence in origin and structure of inflammatory tissue proliferations developing within the various organs or in and upon serous membranes makes it appropriate and justifiable to extend this term to include all inflammatory tissue proliferations consisting of young connective tissue.

When this encloses no other tissue formations, we have a pure granulation tissue which changes into connective or cicatricial tissue, but may also, in special localities, exhibit peculiar properties and produce other connective substance, such as bone, cartilage, etc. When the connective-tissue proliferation is associated with the new formation of other specific tissues—muscles, nerves, glia tissue, epithelium, gland tissue, etc.—we have a mixed granulation tissue, whose final product represents a combination of cicatricial tissue with other tissue formations.

At the height of its development granulation tissue consists of cells, blood-vessels, and more or less large quantities of fibrous basis substance. The cells in general permit the recognition of three main types—larger cells of various shapes with bright vesicular nucleus, smaller uninuclear cells with slightly differentiated, intensely staining nucleus, and multinuclear leucocytes. The relative proportion of these cells is variable; in open granulating wounds we usually find in the deeper parts the large cell forms, in the more superficial layers the smaller cells predominate, and the surface as a rule is covered with liquid exudate and pus corpuscles traversed by threads of fibrin.

Investigations made during the last decades have shown positively that the large cells rich in protoplasm and provided with bright slightly staining nuclei—hence often described as epithelioid cells—are the producers of cicatricial tissue and, therefore, should be designated as fibroblasts (chondroblasts, osteoblasts). It must, however, be emphasized that in the proliferation of granulations not every fibroblast actually produces connective tissue. On the contrary, conditions are very often present which require that a portion of the formative cells, even those capable of developing specific tissue formations, should again perish.

The production of the connective tissue, that is to say, of the fibrillary basement substance, is thus effected: the cells assume the most variable forms—club shaped, fusiform, stellar, etc.—and partly on the protruding ends, partly at the sides, undergo fibrillation which leads to the formation of connective-tissue fibrils; these are derived originally from the cell protoplasm, but later on become separated from it, so that the fibroblast, reduced in bulk, lies as an independent cell on the surface of the newly formed fibre. In the production of osseous and cartilaginous tissue the connective-tissue cells—osteoblasts and chondroblasts—form partly densely fibrous, partly hyaline basis substance, and then the remainder of the formative cell comes to rest in peculiarly shaped interspaces, jagged in the case of bone, more rounded and smooth in the case of cartilage.

The fibroblasts of the granulation tissue are most probably always

derivatives of the fixed connective-tissue cells situated in the inflamed region and undergoing mitotic division. For some length of time the view was very prevalent that also the larger uninuclear blood cells which escape during inflammations along with the multinuclear forms from the blood-vessels were endowed with the same capacity for producing connective tissue. This view appeared justified by the demonstration that fibroblasts occurred also in places which they could have reached only by migration, as, for instance, in porous bodies or in glass chambers with capillary spaces that had been introduced into any living tissue, or else in the interspaces of thick fibrinous deposits upon serous membranes. Since the power of migration at that time was conceded only to the free cells of the blood and of the tissue juices, the occurrence of fibroblasts and the formation of connective tissue at the points named could not be explained otherwise than by assuming a further development of the known wandering cells into fibroblasts.

The knowledge that cells newly formed by mitotic division of fixed cells are likewise capable of motion and migration has deprived the above-mentioned observations of their value as evidence and at the present time most of the authors hold that the producers of cicatricial tissue are all descendants of fixed tissue cells. Still, there are some investigators (Arnold, Metchnikoff) who assume that this function may also be exerted by uninuclear cells emigrated from the blood-vessels and by free wandering cells of the connective tissue. It is impossible to deny absolutely that this may occur, as the methods of examination at our disposal do not always permit us a positive distinction between the larger uninuclear leucocytes and the derivatives of proliferated tissue cells. Moreover, it may well be that derivatives of the fixed tissue cells immigrate into blood-vessels and are then included among the leucocytes of the blood.

The fibroblasts, also designated as granulation cells in the more restricted sense, are as a rule uninuclear cells, the division of the nucleus following soon after the division of the cell. At times, however, we notice in granulations also multinuclear cells (multinuclear giant cells) which may have as many as ten to forty and more nuclei. The formation of such multinuclear cells always points to the existence of special conditions, either a peculiarity of the cause of the inflammation or an unusual course of the process, in isolated cases, also, extraordinary qualities of the inflamed tissue. In the first-named group tuberculous granulations constitute the chief representative; in these giant cells are so frequent that they may be utilized as a diagnostic criterion, though similar giant cells occur also in leprous and syphilitic granulations. The cause of the giant-cell formation is to be ascribed to the bacilli taken up by the cells and in-

creasing in them, which produce partial changes and necrosis in the protoplasm, so that its division is made difficult or interfered with, while the division of the nucleus progresses.

The second group is formed by the giant cells of foreign bodies, that is to say, giant cells developing at the surface of foreign bodies that have penetrated from without, partly also on the surface of necrotic foci. Their origin is probably due to the fact that contact of proliferating tissue cells with the surface of foreign bodies having a certain chemico-physical quality hinders the division of the protoplasm while the division of the nucleus is left unimpaired. Thus, for instance, giant-cell development is regularly observed in the neighborhood of silk ligatures or around hairs that have penetrated into the tissue, while it is usually absent on the surface of fibrinous exudate.

The third group is represented by giant cells identical with normal osteoclasts and which develop in granulating bone marrow and periosteum. As they are situated mainly on the surface of bone trabeculæ and cause their absorption in a manner similar to that occurring under physiological conditions, they may be regarded as related to the foreign-body giant cells, but cannot be exactly identified with them, inasmuch as they appear also at a distance from bone trabeculæ. Finally it is to be noted that giant cells are occasionally met with in the most various tissues, even in epithelium, without the cause of their development being discernible. A tendency to the formation of giant cells is shown especially by proliferating fatty tissue.

The new blood-vessels of granulation tissue arise by the formation of sprouts from the capillaries in the inflamed region, whose parietal cells proliferate with great facility, so that in inflamed tissue the endothelia are very often transformed into epithelioid cells rich in protoplasm and with nuclei exhibiting in part karyokinetic figures. The sprouting process is as follows: on the outer surface of a capillary a tent-like protoplasmic elevation terminating in a fine fibril becomes visible. In its further development this elevation changes to an arch, ending either in a fine free fibril or more rarely in a protoplasmic club-shaped swelling, or else becomes embedded in a previously formed capillary or in a similar protoplasmic arch. Liquefaction beginning either at the point of origin or in the interior of the protoplasmic arch changes this from a solid to a hollow structure, and sooner or later blood enters it from the mother capillary. The offshoot, at first free from nuclei, receives such later on from the capillary wall, when they increase by division and scatter through the new vessel. After a certain length of time the protoplasmic material is divided off according to the distribution of the equidistant

nuclei, so that treatment with silver nitrate will show the marks of cement ridges between the endothelial cells in the newly formed capillary.

So far as is known, a new formation of vessels in granulations occurs only in the manner here described. The statement, that the blood-vessels originate as intercellular canals the result of neighboring cells arranging themselves in rows and becoming joined into a tube which is entered by the blood current, has not been confirmed by incontrovertible observations. The histological appearances described in support of that statement may be explained, at least in part, by the fact that granulation cells apply themselves from without to the sprouting vessels so as to strengthen their walls.

Observations are still lacking as to the transformation of newly formed capillaries into larger blood-vessels, and therefore it is not known from what cells the muscle cells of the media are developed. It is probable, however, that they are derived from the muscularis of the afferent and efferent branches, which are sure to enlarge with the increase of the capillary distribution.

According to what has been stated, the leucocytes of the granulation tissue play no active part either in the new formation of the tissue or in that of the vessels, but they still form a characteristic element of the granulation tissue. Their number varies according to the form and the stage of the inflammation and along with other factors may serve for estimating the intensity of the process—in other words, of the exudation from the blood-vessels. For instance, suppurating granulations contain, especially in their superficial layers, many more leucocytes, particularly multinuclear pus corpuscles, than granulations already covered with epithelium and approaching the end of their development. The persisting emigration may occur both from old and from newly formed capillaries.

Some of the emigrating leucocytes—*i.e.*, those passing to the surface of wound, ulcer, and abscess-wall granulations—are sooner or later lost, desquamated, and disintegrated or cast off externally. Of the leucocytes remaining in the granulation tissue some may enter the neighboring tissue and be carried back into the system by the lymph channels. It is probable that leucocytes may also immigrate directly into the blood-vessels. Still others perish within the granulations and become subject to phagocytosis—that is to say, they are taken up by fibroblasts or other tissue cells present in the proliferating region, such as epithelia, or they may actively penetrate into them.

The engulfing of leucocytes by fibroblasts may be observed even in early stages of the granulation process—for instance, in swollen

connective-tissue cells still retaining their original position—and in the further course it forms a widespread and easily recognized phenomenon. Most commonly we find only one leucocyte, usually of the multinuclear variety, in the fibroblasts, though several may also be taken up gradually by a single cell.

It can hardly be doubted that the engulfing of leucocytes by fibroblasts represents an act of nutrition, and in favor of this view the fact may be cited that appropriate methods of examination will show a gradual destruction of the ingested leucocytes, the protoplasm disappearing first, then the nuclei and their detritus, constituting a digestion of the cells. Nor is it improbable that the fibroblasts by this absorption of nutriment increase their vital energy, so that leucocytes acting as food augment the proliferating power, but this view possesses merely the value of an hypothesis.

When the site of an inflamed focus includes foreign bodies penetrated from without, such as bacteria, or remains of necrotic tissue, or red blood corpuscles and coagulated masses of exudate, these substances may likewise be taken up partly by the emigrated leucocytes, partly by the fibroblasts, and the latter may contain leucocytes which in turn enclose other bodies, like red blood corpuscles or the remains of such and flakes of hæmosiderin.

In all these processes, known as phagocytosis, it is not to be denied that a certain selection is made in the ingestion of the foreign bodies named. Insoluble particles of dust, soot, fragments of coal, cinnabar, etc., are taken up easily and extensively both by leucocytes (microphagi) and by fibroblasts and other proliferated tissue cells (macrophagi). Bacteria are sometimes engulfed by the cells, sometimes not, and the same forms of bacteria are sometimes found uniformly free, sometimes largely enclosed in cells. The cause of this phenomenon is to be ascribed to the fact that bacteria and their products sometimes act on the neighboring mobile cells negatively, sometimes in the sense of a positive chemotaxis. In the former case they prevent the approach of the cells, in the latter they attract them. In many cases this attraction does not occur until the bacteria in the tissue have become decrepit or inert, when they exert an attractive effect on the cells as dead foreign bodies, by means of their proteins.

Very readily absorbed, moreover, are fatty degenerative products of the tissue, such as are furnished abundantly by disintegrating medullated nerve substance, and leucocytes or fibroblasts may take up large quantities of fat globules, so that they change into large globular fat-granule cells in which the nucleus is no longer recognizable without staining. In inflammation of the brain and spinal cord

such fat-granule cells are constantly present during the disintegration of the tissue.

When escaped red blood corpuscles disintegrate in the tissues, it is mainly the resulting ferruginous yellow and brown flakes and granules of hæmosiderin that are taken up by the cells, so that pigment-granule cells are formed. The remains of disintegrated fibrin, however, are not as a rule engulfed by the cells.

The substances taken up by phagocytes may be rapidly destroyed in the interior of the cell, as is the case with bacteria, but many substances resist for a long time—*e.g.*, fat droplets—or remain permanently undissolved (coal dust). Some of the cells loaded with foreign bodies continue in the same position for a long period, and may even be transformed into fixed tissue cells while retaining their inclusions. Some also enter the lymph channels and thus carry the enclosed substances into lymphatics and lymph glands where they are retained and subsequently destroyed or, if indestructible, deposited.

In open wounds the proliferation of granulations and the inflammatory exudation or emigration of leucocytes continue until the external opening is closed in a non-irritating manner by a covering of the granulations with epithelium. The processes of new formation and transformation, however, are not arrested at the same time, but continue for a certain period, and months elapse before the newly formed connective tissue has attained its ultimate development. This development is in general the following: the mass of the fibrillary connective tissue increases and elastic fibres are also formed, while the cells become smaller and at the same time diminish in number. There is besides a partial obliteration of the previously numerous newly formed vessels which are transformed into connective tissue.

The process is similar in the healing of ulcers unless disturbed by some other factors, such as persisting infection or pathological conditions at the bottom of the ulcer. During the healing of ulcerated glands new gland tubules may form within the proliferating granulations.

The healing of lesions in which the tissues whose continuity has been interrupted are placed in apposition—*e.g.*, cicatrizing incised, stab, and gunshot wounds, lacerations, etc.—is effected by proliferating granulations springing from the clefts of the tissue and spreading rapidly towards the breach of continuity. The massiveness of the granulations and the duration of the healing depend, provided infection does not occur, partly upon the nature of the tissue, partly upon the gravity of the lesion and the quantity of the exudate present in the defect and the adjoining tissue. The healing will be most rapid when little or no demonstrable exudate intervenes between healthy wound

margins, since these may be joined directly by germinal tissue when no exudate is to be removed, but even then the time consumed by the healing varies considerably according to the nature and the relative position of the injured tissues.

An interposition of exudate between the wound margins and a marked infiltration of the tissue with exudate cause a longer duration of the inflammatory tissue proliferation, because the exudates, unless removed by the lymph and blood, must be replaced by granulation tissue, the exudate diminishing in proportion as the latter advances.

In inflammations of serous membranes in which the exudate is serous in character the formation of granulations may fail to occur or at least may be confined to insignificant dimensions, and the process soon terminates with the regeneration of such epithelium as may have been lost. Superficial deposits of fibrin that cannot be absorbed determine a longer duration of the inflammation with a consequent proliferation of granulations whose extent and bulk naturally vary greatly in different cases. The proliferation is characterized in general by the fact that it is not confined to the interior of the serous membrane, but extends to its surface, so that granulation tissue projects above it and usually penetrates also into the deposited fibrin which it gradually replaces. The fibroblasts of this germinal tissue are derived from the connective-tissue cells. A participation of the superficial epithelium in the subsequent connective-tissue new formation is assumed by different authors (Cornil, Marchand, Borst, and others), but has not been positively confirmed by the investigations thus far published.

For the final result of the inflammatory tissue new formation the important points are, aside from the peculiarity of the causes of the inflammation, the quantity and quality of the exudate, the position with reference to the vicinity, and the condition of the epithelium. Slight deposits of fibrin that produce no permanent adhesion of opposite layers of the serosa cause merely circumscribed or extensive thickenings of the membrane, which are again covered with epithelium and subsequently acquire a white appearance. Voluminous deposits of fibrin that glue the layers of the serous membrane together produce also more marked connective-tissue proliferations, in the course of which the membranes are sometimes connected by cord and band like connective-tissue adhesions, and sometimes are firmly bound together over their entire extent, so that the process is known as an adhesive inflammation. With close and permanent apposition of two inflamed serous membranes, as is done when they are joined by suture, adhesion may also occur by granulation tissue without preceding material interposition of exudate.

The presence in serous cavities of purulent exudates whose absorp-

tion is usually slow and often cannot be made complete, leads to the formation of granulations covered with pyofibrinous masses on the surface of the serous membranes. When this condition lasts for a considerable length of time, it results in pronounced indurated thickenings of the serosa, together with adhesions at points where opposite granulating surfaces come in contact. The remains of the purulent masses may in this way be enclosed between thickened callous membranes, be shut off from the surroundings, and become inspissated and calcified.

Pulmonary inflammations characterized mainly by accumulated exudates in the air spaces heal by absorption of the exudates and regeneration of the epithelium. The recovery is generally perfect, but proliferations of granulation tissue may occur which cause on the one hand a thickening of the alveolar septa and of the peribronchial and perivascular connective tissue, and on the other hand may also project directly into the lumina of the alveoli. In this event the granulation formation does not differ in principle from pleuritic proliferations, and in intraalveolar formation of granulations after croupous pneumonia the exudate is also replaced by germinal tissue.

The inflammatory tissue proliferations occurring under various conditions in the depth of the tissues—in the skin, in muscles, bones, glands, nerves, in the brain and spinal cord—progress in a manner absolutely identical with the granulation of wounds. In every instance there is a proliferation of the connective-tissue cells associated with an emigration of cells from the blood-vessels, and foci described as cellular infiltrations are by no means always accumulations of leucocytes, but are often true granulating foci. That under such circumstances manifold gross and microscopic appearances are presented is readily explained by the differences in the noxious influences, by the varying nature of the tissues, and by the different stages in which the inflammatory diseases come under observation. In general it may here also be said that in the beginning the exudative processes are most pronounced, while later on the proliferations predominate. Still, conditions may obtain which cause a persistence or a frequent repetition of the exudative processes, as, for instance, by renewed increase and spread in the tissues of inflammation-producing microorganisms. A further complication may also result from the structure of the granulation tissue and the connective tissue springing from it, since, as stated before, special connective substance (cartilage, bone, etc.) may develop or the proliferation of granulations may be associated with the formation of specific tissues. Thus we find in proliferating inflammations of the liver as a rule also a new formation of bile ducts or at least of epithelial cell cords, in inflammation of

muscles a new formation of muscle fibres, in periosteal inflammations a new formation of bone or cartilage, in cerebral or spinal inflammations a new formation of glia tissue.

A special and characteristic deviation from the ordinary inflammatory tissue proliferation occurs when centres of liquefaction and abscesses form within the tissue or when the inflammation has caused larger necrotic foci.

When an abscess has formed, there ensues later on a proliferation of granulations at the margin of the liquefied focus, in a manner exactly like that observed in open wounds or ulcers. When the abscess is small, the pus, the cells of which gradually undergo fatty degeneration and disintegration, may be absorbed or be replaced by germinal tissue, the process healing by cicatrization. When the abscess is larger, it may be diminished by partial absorption and inspissation of the pus, but there will be no complete substitution of connective tissue; the abscess will be simply encapsulated by granulation and connective tissue, the latter constituting the external, the former the internal layers—together called abscess membrane—of the enclosing wall. Abscesses thus encapsulated by a membrane may remain within the body for years and decades; for instance, in the brain, in the liver, in the kidneys, in the lymph glands, or in the testicle. Inspissation and calcification of the contents produce in course of time a permanent termination of the disease. On the other hand, when the parietal granulations elaborate secretion—*e.g.*, in hepatic or cerebral abscesses—the encapsulated abscess may also enlarge owing to augmentation of the liquid contents. Moreover, as long as infectious microorganisms are present an extension of the inflammation to the neighborhood is not impossible. Finally, the wall may suppurate and rupture.

Conditions resembling those of abscesses are presented by collections of pus in closed mucous canals; for instance, in the uterus with impervious external or internal os, or in the Fallopian tubes when their abdominal ostium has been occluded by preceding inflammation with consequent adhesion to neighboring structures. Here, too, pus sacs form which may persist for years, enlarge by secretion from the wall, set up inflammation in the vicinity, and occasionally rupture.

When considerable tissue necroses have developed, there are formed at the limit between the living and dead material an inflammation and a proliferation of granulations which produce a detachment, a sequestration of the dead from the living tissue; sometimes, according to the etiology of the process, chiefly by suppuration, sometimes mainly by proliferating granulations. Soft tissues may be dissolved by the two processes, but bone substance resists the sup-

purative process and can be made to dissolve only by living tissue. When this occurs, multinuclear cells, so-called osteoclasts, usually appear near the liquefying bone.

When the detached necrotic tissue—*i.e.*, the sequestrum—lies at the surface, it is cast off by the organism, an ulcer remaining which is more or less completely closed by proliferating granulations. Necrotic foci developing in the interior of the tissues are absorbed in the course of time when this is possible and are replaced by granulation and connective tissue. Larger necrotic masses that are resistant to absorption are encapsulated by connective tissue, the unabsorbed remnant not rarely becoming calcified.

When dead tissue undergoes simple liquefaction without being replaced by cicatricial tissue, as happens, for instance, not uncommonly in the brain, the result is a cyst—*i.e.*, a cavity filled with fluid and limited by a wall.

In the case of bone necroses incapable of absorption the encapsulating membrane, being derived from the periosteum or the bone marrow, usually forms bone that firmly encloses the sequestrum in a case. The interior of the cavity as a rule contains, besides the osseous sequestrum, some pus, so that it represents an encapsulated abscess enclosing a necrotic piece of tissue.

The Significance of Inflammation.

If we define an inflammation as a tissue degeneration associated with pathological exudations, in the course of which proliferative processes likewise occur, we can regard it as nothing else than a pathological state of the tissue whose peculiarity is due on the one hand to the special effect of the cause producing the inflammation and on the other hand to the vital qualities of the affected tissue.

During the last decades various authors have discussed the question whether inflammation is an appropriate process. Leber maintains that all processes connected with inflammation bear the character of appropriateness. He assumes that the action of external noxæ incites certain vital activities of the organism, which serve in the defence against the former and in the removal of their sequelæ. He looks upon inflammation, therefore, as a struggle of the tissues and organs of the body against the effect of noxious substances, particularly against parasitic intruders. Neumann endeavors to comprise under the term inflammation all the phenomena developing locally after primary lesions and tending to the healing of these lesions. He distinguishes, as stated above, a primary effect which is directly produced by the cause of the inflammation, secondary disturbances rep-

resenting the consequences of the primary effect, and a reaction that is to say, processes which again remove the primary effect and the secondary disturbances. According to him, the phenomena occurring after tissue lesions, despite their extreme variety and multiplicity, are governed by a general principle: "For it is unquestionably true for many cases that they take a course which seems to answer best for the purpose assumed, namely, the restoration of tissue continuity, and that they adapt themselves to the causes of inflammation in a manner resembling that by which the digestive activity of the intestinal canal is modified by the composition of the ingested food." Metchnikoff goes much farther in that he, without regard to those morbid vital phenomena recognized of old as the characteristics of inflammation, identifies inflammation with phagocytosis, and interprets this phagocytosis as a struggle of the organism against external noxæ, especially against infections. Metchnikoff's presentation did not remain without some influence upon the interpretation applied to inflammatory processes, particularly those occurring in the course of infections, and there has been no lack of authors who have defended the theory of the phagocytic struggle. Nevertheless, this doctrine is in every way erroneous, both because the actual conditions do not correspond to it and because the vital processes here in question have been falsely interpreted; in other words, because it no longer rests on the foundation of a naturalistic view of the processes of life.

In the first place, phagocytosis is a phenomenon which occurs by no means in every inflammation; on the contrary, it is entirely absent in numerous typical inflammatory processes. Accordingly it cannot by regarded as an essential and characteristic part of inflammation, and if Metchnikoff identifies phagocytosis with inflammation he applies this term to vital processes which in no way correspond to what hitherto has been described as inflammation.

Phagocytosis is a process which has long been known. It has been a familiar fact for decades that not only the motile cells of protozoa, but also the motile cells of the more highly organized multicellular animals may take up in their protoplasm small particles. In the year 1875 I described at length the phenomena of phagocytosis occurring in inflammatory proliferating granulations, in particular the ingestion and destruction of leucocytes by fibroblasts. In general, phagocytosis has been interpreted as an act of nutrition, that is to say, as an attempt of the cells to feed themselves with these particles, and it is beyond question that the process is to be regarded in this light, even when the ingested substance is of no use to the cell or is indigestible and perhaps also injurious. Metchnikoff, who has occupied himself with this subject since 1882, has infused into these

vital phenomena the idea of a struggle, mainly because he has traced them in infectious diseases. Such an interpretation lacks every scientific foundation. When motile tissue cells in the course of an inflammation take up fat droplets, flakes of hæmosiderin, particles of dust, etc., it is impossible to understand how this can be interpreted as a struggle which presupposes an opponent. His idea appears more reasonable when we speak of a struggle of the tissue cells with bacteria, in which case, indeed, the interests of two modes of life are in collision. Still, even here the comparison of this collision to a struggle between two opponents can at most lay claim to being a poetical description, but not a naturalistic view of a vital process. In such a case there is no question of a purposive struggle of two individuals with each other. All the processes observed in this connection are solely vital manifestations necessarily resulting from the living qualities of the respective cells and microorganisms. In amœboid cells external influences, dissolved chemical substances, and contact with solid bodies produce movements of the protoplasm which may lead to the incorporation of small corpuscular elements. Phagocytosis in infectious diseases, however, presupposes that the motile cells are stimulated by the above-named influences to migrate towards the bacteria and to ingest them. These influences emanate from the bacteria themselves and must be of such a nature as to stimulate the phagocytes to the act of phagocytosis. In what the supposed struggle is to consist in this process does not appear. At most we could speak of a struggle if the bacteria exerted such an influence on the neighborhood as to prevent the phagocytes from approaching and engulfing them, but even then it is impossible to attribute to the participants an act of the will, a definite purpose necessary to a contest; on the contrary, we are forced to assume that it is nothing but the qualities of the bacteria which bring it about that the cells are not incited to phagocytosis or else are hindered in making the change of shape necessary for it.

If after what has been set forth above inflammation cannot be identified with phagocytosis, and the latter cannot be regarded as the manifestation of a struggle, then the further corollary that phagocytosis is always something appropriate and useful for the organism is an unjustifiable assumption. When the cells take up, kill, and destroy vigorous bacteria capable of multiplication, the usefulness of the process appears unquestionable. When bacteria which have been weakened or killed by other means in the organism are then completely destroyed by phagocytosis, the value of the latter may be disputed. When the bacteria find in the cells a suitable place for multiplication or are carried away by wandering cells without being killed,

then the phagocytosis bears the character of a noxious process and absolutely no appropriateness can be granted to it.

But what about the remaining processes occurring in the course of an inflammation? Can we ascribe appropriateness to them? Leber, Neumann, and others think so, but an objective consideration of the inflammatory process shows that a positive appropriateness for all cases is out of the question. Such an assumption is wide of the mark, and would presuppose the presence of an appropriate and purposively acting natural healing power for the substantiation of which no reasons can be adduced. An absolute appropriateness might be most readily ascribed to the regenerative processes following after inflammatory tissue lesions, but these tissue proliferations do not appear in all inflammations, nor are they always of use to the individual in question; besides, their occurrence is not governed by the laws of appropriateness, but is merely the necessary consequence of the vital qualities of the tissues which under certain conditions have the power of producing new cells and new tissues. Whether or not this production leads to something useful depends not only upon the respective cell, but also upon the state of the surrounding structures and to a considerable extent upon the nature and variety of the cause of the inflammation. All the other vital phenomena manifested in the course of an inflammation, the tissue degeneration and the pathological exudations, owe their peculiarities in part to the qualities of the noxious agent, in part to the qualities of the affected tissues. What a difference there is in the course of an inflammation when infections are present which produce local inflammations! Staphylococcus pyogenes aureus and streptococcus pyogenes cause mostly suppuration, but on mucous membranes and in the lung also croupous inflammations. For the typhoid bacillus necrosing inflammations of definite portions of the intestinal wall and eventually also of the mesenteric lymph glands are characteristic. The tubercle bacillus gives rise to proliferating granulations which terminate partly in caseation, partly in induration. In lepra caseation is absent in the granulating foci. In actinomycosis suppuration is associated with extensive tissue indurations. All these typically recurring peculiarities of the respective inflammatory process are not determined by reasons of appropriateness, but represent phenomena resulting of necessity from the qualities of the cause of the inflammation in its action on the affected tissue. An appropriateness could be granted to them only if it were possible to demonstrate that the resulting processes are in all cases especially apt to prevent the morbific agents from spreading and to kill them.

The attempt has been made to furnish this demonstration. It has

been asserted that in these processes a phagocytosis occurs by which the bacteria are killed; further, that the accumulating cell masses form a wall around the bacteria which mechanically prevent their spread; finally, that the cells secrete bactericidal substances and antitoxins that kill the bacteria or render their products harmless, etc.

It is not to be questioned that all the processes named actually occur and may exert a favorable influence upon the disease; but it does not follow that this is always the case, nor that these processes constitute the most important or the most appropriate measures for the protection of the organism against the infection in question. Bacteria often perish in the body without the aid of inflammatory processes, and in inflammations following after infections the destruction of the bacteria does not always occur at the point of the inflammatory cell accumulation. We may observe, as stated before, that exudate cells or proliferated tissue cells transport bacteria through the body, and there are microbes (lepra bacilli) that find in the cells a suitable soil for their development and multiply in them. Therefore the cell accumulations in infectious inflammations cannot in every case be regarded in the same light, but their importance must be determined for each kind of infection, and at the same time it must be borne in mind that their importance varies according to the gravity and the location of the infection. When in infectious catarrhs the cells migrating to the surface remove the bacteria, this may exert a favorable influence upon the course of the disease, but this cannot be said of the accumulation of pus corpuscles in the larger body cavities, in the tissue parenchyma, etc., or would be true only if it had been demonstrated that the cells cause the death of the bacteria. Still more doubtful is the value of the serous, fibrinous, and hemorrhagic exudates and of the tissue degenerations. Liquid transudations on the surface of mucous membranes may occasionally wash away the inflammation producers and weaken their effect. Collections of fluid in the body cavities or in the ventricles of the brain cannot serve this purpose, but on the contrary often act injuriously upon the neighboring organs. Not rarely, too, they furnish a fertile field for the multiplication of noxious microorganisms, both those acting from the first in the production of the process and those secondarily superadded. Fibrinous and cellular exudates in the lung impair its function, often to the point of insufficiency. Croupous exudates in the pharynx and the air passages interfere with deglutition and respiration and form, besides, a favorable medium for the development of bacteria. No appropriate character can be ascribed to the partial destruction of the epithelium of the mucosa and of the

skin in different forms of inflammation, but it represents rather an injurious tissue lesion which contributes little towards the removal of the cause of the inflammation, while it deprives the mucosa and the skin of their protective epithelial covering.

When poisonous substances or bacteria are excreted by the kidneys, the process is indeed a salutary one, but only in so far as the kidney is still able to perform such excretory function. With the onset of degenerations of the glandular parenchyma and with the occurrence of pathological exudates from the glomeruli or from the interstitial capillaries an impairment of the renal function is brought about that can be of no use whatever. Every inflammation of the liver, of the muscles, or of the heart which injures the specific parenchyma also damages the function of the organ, while no salutary phenomenon is to be recognized either in the tissue degeneration or in the exudates.

From the examples here enumerated, which could be increased *ad libitum*, it is made sufficiently clear that in the course of inflammations many phenomena occur which are without any use whatever. This remark applies not only to the tissue lesions immediately due to the inflammation, but also to the alterations following it secondarily, to the so-called reaction of the organism to the noxious influence. The teleological mechanics of organized beings formulated by Pflüger, according to which the cause of a want at the same time furnishes the cause of its satisfaction, do not apply to pathological processes such as characterize inflammation. There is no appropriate and purposive vital or natural healing power which in the various tissue lesions is always capable of evoking the suitable counteraction. The elements directly or indirectly acted upon by the lesion respond to the latter by alterations and activities whose form and effect are founded in the organization and the vital qualities of the tissues involved, but are not determined by reasons of appropriateness. Accordingly the question, Is appropriateness to be ascribed to inflammation? is not one that can be answered in a general way, because nothing is to be said about it that would apply throughout. In the course of the inflammation inappropriate and appropriate vital phenomena alternate, and a certain process, such as, for instance, the emigration of leucocytes or the proliferation of the tissue cells, has not always the same value during the inflammatory disease in question.

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ERYSIPELAS.

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ERYSIPELAS.

History.

The history of erysipelas and our knowledge of it represents, in a degree, the history of medical science itself. It shows, at the same time, the development of medicine from its earliest stages up to the present. Medicine had to cease to be an art and become a science before any progress in the knowledge of infectious diseases generally, and erysipelas especially, could be made. Hippocrates (460 to 377 B.C.) was nearly as well acquainted with this disease as were the moderns up to the middle of this century. This, at least, is true so far as the clinical symptoms, diagnosis, epidemiology, and treatment are concerned, though in earlier times doubtless some other diseases of similar character were confounded with it. Hippocrates, in his "Epidemics," Book III., describes an epidemic of erysipelas so well that we are able to recognize the disease in all its different stages as we know them to-day. Celsus also describes a typical disease complicating wounds or making its appearance apparently as an idiopathic disease, and though the treatment he prescribes sounds strange enough, it surely is just as scientific as that of a thousand years later, and most probably just as effective as all the countless other remedies employed up to recent years, to the time when methodical treatment by means of antistreptococcus serum was suggested. For those who are interested in the history of medicine, I here insert a translation of a typical paragraph of Celsus' treatise on "Erysipelas."

"That affection, which I stated to be called ἐρυσίπελας (erusipelas), not only supervenes upon a wound, but occurs without one, and sometimes carries with it considerable danger, especially if it fix itself near the neck or head. If the strength permit, it will be expedient to let blood; the next measure is to apply poultices, at once repressing and refrigerating; particularly ceruse with the juice of nightshade, or Cimolian chalk mixed up with rainwater, or flour incorporated with the same, to which may be added cypress, or if the part be tender, lentils. Whatever is employed should be covered with a beet-leaf and laid upon a piece of linen rag moistened with water. If refrigerants are not sufficiently efficacious alone, a mixture is to be made as fol-

lows: of sulphur p. X. i., ceruse and saffron, of each p. X. xiiss.; these are to be triturated together with wine, and used as an unction; or, if the part be less tender, the powdered leaves of nightshade are to be mixed with hog's lard, and applied over the part spread on linen.* But if there be a blackness which has not yet begun to spread, mild corrosives are to be applied; and the ulcer, when clean, is to be nourished as in any other case. When there is a higher degree of putrescency, and it advances and spreads, more powerful corrosives are necessary. If these fail to subdue the malady, the part ought to be cauterized until moisture no longer flows from it; for sound flesh when burnt becomes dry. After the cauterization of a putrid ulcer such applications are to be used as may detach the sloughs, or eschars as the Greeks call them. When these have fallen off, the ulcer must be cleansed, and that preferably by honey and resin; although it may also be deterged by other medicines used for dressing suppurating surfaces, and healed by the same method."

Galen was the last author of that time who described erysipelas accurately, but his followers lost themselves in elaborate speculations as to the nature of the disease; and this state practically existed up to Schwann's time. The prominent leeches of the sixteenth and seventeenth centuries believed that the genesis of erysipelas was accomplished through the agency of the bile (bilious erysipelas). Choleric and full-blooded individuals were specially susceptible. Some physicians differentiated two forms of the disease, one in connection with the bile and the second in connection with the blood. The latter offered a better prognosis than the former, and was observed at times when an envenomed air prevailed.

This conception of the disease remained until the beginning of the present century, when the reports of epidemic erysipelas were of more value. They were, at least, exact reports of facts well described, and not mere speculations as to the etiology with fantastic prescriptions for treatment of a disease which scorned all therapeutic efforts as futile so long as its real etiology was unknown.

Those outbreaks which occurred in all forms, from the mildest to

*In the above, p. stands for pondo, which is an indeclinable word, and when joined with numbers signifies libra or a pound; when with other weights, it stands for no more than pondus or weight in general. X is the denarius mark, which contained originally ten asses. This by the copiers has been often confounded with X, denoting the number of ten denarii; so that after all the pains of critics and commentators the proportions of the ingredients in several compositions seem to have been irrecoverably lost. For this reason I suppose the later editors have thought fit to replace the sign with the ordinary asterisk. One denarius makes six sextants = three scruples. The above prescription would read thus: of sulphur one denarius, ceruse and saffron, of each twelve and a half denarii.

the most malignant types, between 1830 and 1860, at different places in Europe (Scotland, Denmark, Germany) and in North America, are especially interesting. I may state here that the first epidemic of erysipelas in the United States did not occur in 1843, as is generally believed, but that the epidemic of smallpox in 1699 was accompanied by erysipelas, as Haser, in his "History of Epidemic Diseases," abundantly proves. European, and especially German literature, which treats of other epidemics very fully, seems to have taken but little notice of those in the United States. Among the reports of American physicians, those of Drake, Peebles, Shipman, G. Sutton, Charles Hall, G. Dexter, and others deserve special notice. We find the first traces of a pandemic—especially of the so-called *typhoid erysipelas*—in Canada, in the year 1841, whence the affection spread over the whole territory of the United States, mostly towards the southwest. The intensity and extent of this so-called typhoid erysipelas varied greatly. Sometimes the disease occurred more or less generally in a particular locality, while at other times the cases were only sporadic, or were restricted to hospitals. Drake, in his excellent treatise, describes the course of the epidemic thus:

"After having started in the winter of 1826 in Burlington, Vt., in 1832 in Ogdensburg, N. Y., in the spring of 1833 and winter of 1836 in St. Clairsville, the general outbreak of the great scourge occurred in 1841, when the affection first manifested itself in Canada. Thence it came in the following year to New York and Vermont, and at the same time to Indiana. The winter of 1842–43 brought it to Missouri and Ohio, and in the winter of 1843–44 the epidemic reached its height and largest distribution in Canada, Wisconsin, New York, Indiana, Illinois, Kentucky, Tennessee, and Mississippi, while the following spring showed only Missouri, Alabama, Tennessee, and New York infected. In the latter States the epidemic slowly died out until 1849, so that in the winter of 1849–50 we find reports only from Vicksburg, New Orleans, and a few other places. The spread of the disease was from northeast to southwest, through fifteen degrees of latitude; many places in the infected region remained entirely free from the contagion."

We must not forget, however, that a number of the highest authorities do not believe in the erysipelatous character of the epidemic just mentioned. Men like Hirsch and von Volkmann have grave doubts whether a good many of these cases were not more of a diphtheritic nature than truly erysipelatous. We must bear in mind that those who observed this epidemic had to base their diagnosis entirely on the clinical symptoms, and did not have the absolute bacteriological proof of its nature, so easily accessible nowadays to any student

of medicine. Therefore, with all respect to the great abilities of the above-mentioned authorities, we have to leave in doubt whether some other diseases, especially diphtheria and dysentery, were not confounded with erysipelas, though it is beyond question that, even if this were true, in a great many cases these diseases were complicated by erysipelas. It is only fair to add that Tillmanns, in his admirable treatise on erysipelas, is all but convinced of the truly erysipelatous character of this most interesting epidemic, which is unparalleled in medical history.

Etiology.

While in former times the clinical features and epidemic character of disease excited the special interest of physicians, the question of the causative agent (the contagium vivum) has come into prominence since the beginning of the bacteriological tendency in medicine. As has been the case with most of the infectious diseases, the bacteriological investigation of erysipelas has also been crowned with success. Its microbic nature was made probable by the discovery of cocci found in the skin, lymph, and blood of patients with this disease.

Bacteriology.

Nepveu (1870) was the first to describe cocci found in the blood of erysipelas patients. Whether these cocci really were the true erysipelas cocci remains doubtful, as the latter are to be found in the blood, if at all, only exceptionally. Later on, Volkmann, Wilde, Orth, von Recklinghausen, Billroth, Ehrlich, Luckomsky, Klebs, Tillmanns, and M. Wolff also described the cocci; but this was during the period from 1870 to 1880, when our modern ideas about the etiology of diseases had gained ground, though an absolute result was unattainable with the methods of examination then in existence. The reason why we could not get beyond the probability that microbes which we saw were really the specific agents of erysipelas, was that the direct proof was still wanting. The latter was not possible until Koch's great discovery of a solid, transparent nutrient culture medium and the modern development of bacteriological technique, permitting the differentiation of various bacteria and their cultivation in pure cultures which could be used for experiments on animals. After this was established, it was Fehleisen who described, in 1882 and 1883, his *streptococcus erysipelatis*, as the specific cause of the disease in question. This was proved beyond any reasonable doubt, as he could fulfil the three particular demands of Koch's doctrine. He found a microbe constantly in the lymphatic system of an erysipelatous area

of skin; he could cultivate this in pure cultures outside of the human body; and, lastly, he could produce erysipelas by inoculations with cultures, not only in animals, but also, what is vastly more important and conclusive, in man.

The exposition of the etiology of erysipelas is very simple and short, if we admit the modern point of view, and accept what the whole scientific world has accepted. The definition may be condensed into one short sentence: *Erysipelas in man is caused by the action of the chain coccus, identical with streptococcus pyogenes, which causes suppuration in various parts of the body, from a simple abscess of the skin to fatal peritonitis, and which may also be the cause of septicæmia without suppuration.*

We have to assume that this difference of action of the cocci upon the human tissue depends upon the locality where the bacteria enter and propagate, as well as upon the degree of virulence of the micro-organisms, and the varying power of resistance of the body attacked.

Formerly the streptococci found in erysipelas, in suppuration, in septicæmia, in puerperal fever, and in other inflammations, were taken for different species, and described as specific causative agents of the diseases named. Various authors thought that they had found certain constant differences of species. This opinion was backed by those who held to a pure pathological and anatomical standpoint in bacteriology, who called attention to the heterogeneous processes caused by streptococci. They assumed that one species of streptococcus could produce only erysipelas, another only suppuration, a third only sepsis, and so on; but this opinion has now been practically abandoned. Most bacteriologists maintain that the cocci forming long chains, which are found in the different streptococcal affections of man, belong to one species, for which Fluegge proposes the name *streptococcus pathogenes longus.* The identity of those different cocci has been proved by careful experiments on animals, exact bacteriological examinations, and observations of streptococcal infections in man.

The streptococci are cocci of spherical form, without independent movement, about 1 μ in diameter, larger than the staphylococcus, and eaily stained after Gram's method. It is characteristic, further, of this species of cocci to divide continually in the same direction, and to form chains of eight or ten or twenty and more links; frequently the chains are united in fine loops to form larger masses. Besides this chain form we also find the microorganisms occurring as diplococci. Then they cannot be differentiated from other pus cocci, such as staphylococci, until cultures are made. Sometimes we find in a chain a few cells larger than the others. Such larger elements are

especially frequent in older cultures, and are to be considered as forms of involution.

Nutrient gelatin plates are poorly adapted for the culture of streptococci. They grow on them but slowly, and form only after several days round granular colonies which are yellowish-brown when examined under a weak power, do not liquefy the gelatin, and never grow to a large size.

Fig. 19.—Streptococci Chains, Before and During Division. High magnifying power. (After Lehmann and Neumann.)

Agar also is not a good nutrient for streptococci, but we see after twenty-four hours grayish-white transparent or translucent discs, about 1mm. in diameter, which appear under a magnification of thirty to a hundred diameters as colorless masses forming a network of fine loops and meshes. The colonies are a little more turbid and opaque.

On *solidified blood serum*, the streptococcus grows about the same as in other nutrient media. On potato, it does not seem to grow at all. It is of importance to see that the culture medium is slightly alkaline.

In cultures of the cocci grown in *bouillon*, decided differences are possible. Some streptococci cloud the bouillon evenly, with others white flakes and crumbs grow out from the diffused cloudiness and fall to the bottom, while the bouillon above becomes clear again. In most cases the nutrient bouillon is absolutely clear after twenty-four hours. The cocci are united into flakes which adhere to the sides of the glass or accumulate at the bottom.

The streptococci are quite resistant to external influences, such as disinfection, exsiccation, and the like. Desiccated cultures usually remain viable for a longer time than cultures in humid or liquid media, for instance bouillon, in which they die after from five to ten days. To keep streptococci under the best possible preservation of virulence, it is best to use gelatin stab cultures, transferred every five days, and to keep the same in a dark ice-chest.

Marmorek found that the virulence, which usually decreases in cultures very rapidly, is maintained best in a mixture of one part weak bouillon to two parts ascitic or pleuritic fluid, or blood serum from man, horse, or mule.

After several days' growth of the streptoccoci on solid and liquid media, acids are formed; that is, we are able to prove a diminution in the alkalescence of the medium. Possibly the speedy death of the cultures is explained by this phenomenon.

In man the streptococcus creates, besides erysipelas, a number of local and general diseases. Clinically, the fever curve is especially

characteristic, forming a jagged line, with deep and steep interruptions, caused by the morning remissions (Chart No. 18). This is regarded as the typical streptococci curve.

FIG. 20.—Streptococcus Pyogenes × 1000. Smear specimen of sediment of bouillon culture two days old, obtained by the implantation of small pieces of the spleen of a mouse. The animal had died after inoculation with streptococci taken from the fluid of an empyema. In the upper part of the field we see the Y-like mode of division of the chains. The connection of the single cells by a pale plasmatic substance is just visible. The difference in the size of the parts of chains is very clear. (After L. Heim.)

The proof of the presence of cocci is very often possible, simply with the microscope. It is then sufficient to make smear preparations on a cover-glass, treated with diluted Ziehl's fluid or with methylene blue. To find the cocci microscopically in tissue, it is best to stain the sections with Kuehne's preparation, or after Pfeiffer's universal method. Whenever it is not possible to employ the microscopical proof, we may demonstrate the cocci by cultures on inclined agar, at a temperature of 37° C. To obtain the cocci from human erysipelas, Fehleisen recommends the excision of a small piece of skin from the well-defined edge of an erysipelas marginatum, and to put the same in a test tube with nutritive gelatin. The tube is kept for two hours at 40° C., so that the gelatin is liquefied and comes into close contact with the piece of skin; it is then left for a time at a temperature of 20° C., and the contents are finally poured into a Petri flask.

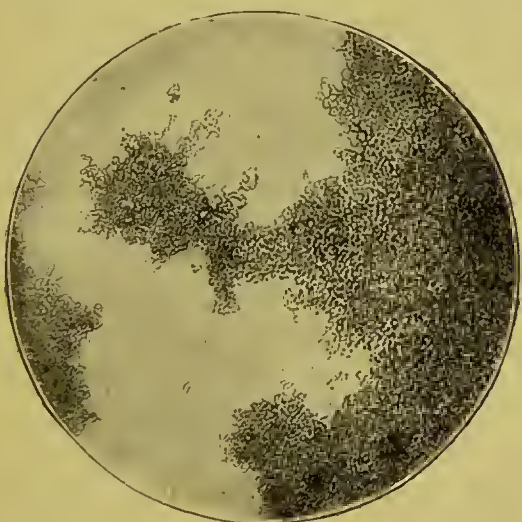

FIG. 21.—Streptococcus Pyogenes. × 100. Two-days-old agar streak culture from the pus in a case of cellulitis pedis. The mesh-like apposition, especially at the edge of the small colonies, is characteristic. (After L. Heim.)

To find the cocci in the blood of septic patients, microscopical examination of the blood is never sufficient, but cultures are always necessary, and even then large quantities of blood have to be disseminated (Petruschky). Another

method is to take from the patient, under aseptic precautions, from 10 to 20 c.c. of blood and to inject a part of the same into the peritoneum of a mouse. If the injected streptococci are not virulent, the injection is borne without any special symptoms. In the other case, the mouse dies at the end of from twenty-four hours to a few days. The most important symptoms of the animals are agglutinated eyes, swelling of the glands, putrid peritonitis, enlargement of the spleen (which is dotted with a smaller or larger number of yellow spots), of the liver, and of the kidneys; the streptococci are also found in all the other

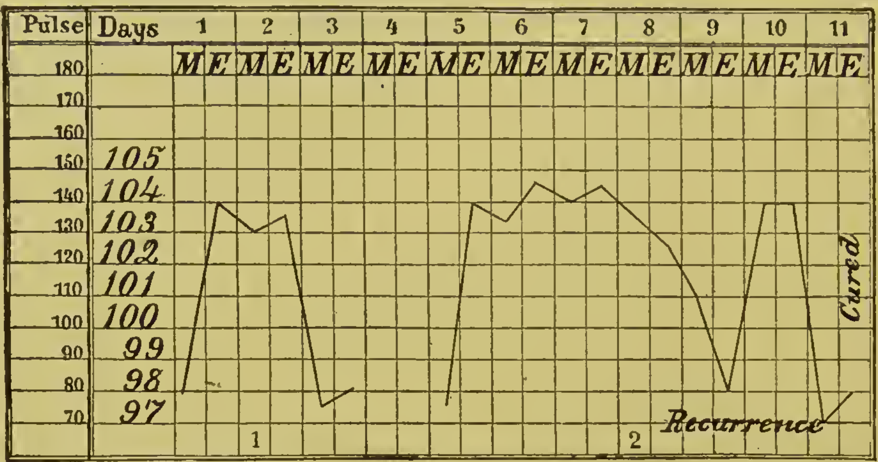

CHART No. 18.—No. 1. Temperature Curve in a Case of Erysipelas of Two Days' Duration with Typical Quick Defervescence. No. 2. Temperature curve in a case of erysipelas with recurrence after transient defervescence.

organs. An exact anatomical and pathological examination regarding the streptococcal infection of mice has been made by Singer and described in his dissertation.

As is well known, blisters on the skin are very frequently formed in erysipelas, which are filled with a clear serous fluid. Although it seems as though we might easily obtain streptococci of erysipelas from these blisters, they usually yield a very poor crop. Nearly without exception this fluid is sterile, if the skin and the instruments used are absolutely sterile. This has been proved by Fehleisen and others.

The latest and most important proofs of the etiological rôle of the streptococcus are the successful experiments to produce erysipelas in man and animals, by transferring pure cultures of the cocci. Fehleisen has inoculated men with streptococci which he obtained from the erysipelas of man, and which he had transferred seventeen and more times from one nutritive gelatin to another. This inoculation caused typical erysipelas. The experiments were performed on patients suffering with inoperable malignant tumors, such as lupus, carcinoma, and sarcoma, and were justified by the experience that certain of these tumors improve, or even disappear entirely, after the patient has acquired erysipelas accidentally.

Clinical Etiology.

The locality where most cases of so-called spontaneous erysipelas occur is the face—that is, a part of the body which is exposed, uncovered, to wind and weather, and to other injurious mechanical and chemical influences of all kinds. If the face were examined daily with a magnifying glass, there would always be found lesions of the skin big enough for the invasion of the poison. Besides, a great many cases of erysipelas of the face represent a continuation of an erysipelas existing in the mucous membranes of the cavities of the head, especially of the nose. This fact has not been taken sufficiently into consideration by the advocates of the spontaneous genesis of erysipelas. That this erysipelas of the mucous membranes of the nose is also not spontaneous is a matter of course, easy enough to understand if it be remembered how many persons have the habit of boring the fingers into the nose, which is the most frequent source of erysipelas of the face. Furthermore, it must be considered that erysipelas does not necessarily start or make its appearance at the point where the lesion of the integument exists. It quite frequently shows itself at a certain distance, the virus wandering through the lymphatic ducts until it finally becomes arrested. How easily these first lesions, the place of entrance, may be overlooked, everybody knows who has the opportunity to observe other septic infections of a phlegmonous character. We see every day most severe phlegmons start from a little scratch, such, for instance, as butchers get from handling meat and bones. The cause of infection is clear enough here, though very often we are hardly able to find the primary lesion. It frequently is healed up in from twenty-four to thirty-six hours, in spite of the infectious character of the disease, which is severe enough to infect other more remote parts, or even the whole system. Or, to pick out another instance, we very often observe the so-called idiopathic bubo in the groin, an adenitis which has its cause in a badly cut corn of the toe, or in a slight soreness of the toes produced by hyperidrosis (sweating feet).

Fig. 22.—Streptococci Erysipelatis. × 700. Section through a lymphatic duct of the skin. (Flügge.)

Kruse, in Flügge's "Mikroorganismen," says: "The streptococci

of these (the nasal) mucous membranes are most probably not infrequently the source of erysipelas of the face, whose start is very often from the entrance of the nose."

It has been said that the possibility could not be denied *a priori*, that in rare cases erysipelas might originate in lesions of the digestive apparatus, the uterus, or the lungs, or, generally speaking, of the internal integuments of the body which communicate with the outer air. This, then, might produce a metastatic erysipelas of the skin. After careful study of the whole literature on this point, I am inclined to say that we have not a single reported case which proves with absolute certainty an infection in this way, though the conception is perfectly correct that streptococcus pyogenes stored anywhere in the body may produce at other parts any other disease, for which the bacterium in question is pathogenic.

The extremely interesting question whether the cocci of erysipelas can enter the body through its natural openings, the uninjured sudatory and mucous glands and hair follicles, is not so easy to decide. Since it has been shown experimentally that microorganisms can leave the body through these natural openings, it cannot be denied, without further investigation, that they are able to enter by the same channels. The experiments above alluded to prove the existence in the sweat of pigs of the same microbes with which they had previously been infected. Of course, the snout, through which alone the pig sweats, had been thoroughly disinfected, the animal being treated with pilocarpine to excite profuse sweating. Furthermore, Garré, professor of surgery at the University of Tübingen, has proved with absolute certainty that infection by the staphylococcus pyogenes aureus through the uninjured skin is possible. He took a small particle of pure culture of the coccus and rubbed it on his forearm, whereupon he got no less than twenty-nine furuncles of the severest kind, the experiment nearly costing him his life.

We might mention here that, while the streptococci are usually transported by way of the lymphatic vessels, it cannot be doubted any longer that the cocci, or at least their toxins, are, under certain circumstances, absorbed and carried on by the blood-vascular system. This was proved beyond any question, by Brieger and Fraenkel, who succeeded in isolating highly poisonous albumins from the urine of a patient with erysipelas. Eight hundred cubic centimetres of urine were treated with alcohol; the sediment was then dissolved in physiological salt solution and dialyzed for twelve hours, to remove the salts. The dialyzed fluid was then brought to the original volume of 800 c.c. Half a cubic centimetre of this sufficed to kill mice within two hours, and guinea-pigs within two days.

Erysipelas in coincidence with internal diseases, acute as well as chronic—as, for instance, typhoid fever, variola, varicella, intermittent fever, pneumonia, Bright's disease, cirrhosis, heart disease, intestinal disorders, etc.—was formerly of especial etiological interest. With our present idea of erysipelas, we can hardly understand that such excellent observers as those who described these cases were not able to keep the two diseases apart, since they had nothing whatsoever to do with each other. This is one of the great results of our modern study of the etiology of diseases, that we know exactly the symptoms which can be produced by a specific disease, and can differentiate other coincident symptoms which have nothing to do with the original malady, and can ascribe them to their proper causes. It cannot surprise us to-day that out of one hundred or one hundred and fifty patients with typhoid fever, some of whom will have bedsores, one should develop the symptoms of erysipelas, starting, of course, from the ulcer; and we should never think of constructing a complicated explanation of this phenomenon. There is quite an extensive literature, with exact statistics, upon the concurrence of erysipelas with typhoid fever and relapsing fever, which is entirely without value for us. We cannot be surprised either to find reports of erysipelas starting from the point of administration of a hypodermic injection done without the necessary aseptic precautions, since that is really a true bacteriological inoculation experiment in man.

It is hardly necessary to go through the other diseases mentioned above, which may occur with erysipelas; but it seems to me that one point should not be omitted, and that is, the *connection of erysipelas with puerperal fever*. It is sufficient to mention the names of Ingleby, Hutchinson, Levergood, Clarke, Storrs, Simpson, Graves, Minor, Hincks Bird, Kneeland, Elkington, Hodge, Wilson, Spencer Wells, Squire, Tilbury Fox, Nunneley, Trousseau, Masson, Hadry, Virchow, Hirsch, Rust, and a great many others, to show what able authorities have directed their attention to this combination.

It is somewhat remarkable that is only within the present century that the identity of erysipelas with some forms of puerperal fever has been accepted, since it is obvious that the puerperium is especially favorable to erysipelatous infection, if we only think of all the lesions, lacerations, and abrasions on the labia, in the vagina, and at the cervix uteri, and especially of the large wound in the uterus itself at the insertion of the placenta. The close relations which are said to exist between erysipelas and puerperal fever may be formulated thus: Whenever the conditions in hospitals, lying-in hospitals, etc., are such that we find epidemics of puerperal fever, there is just as much chance for erysipelas as for any other wound complications, so-called puerperal

fever, septicæmia, etc., as all these infections are brought about, not by any impalpable virus, as poisonous air, but by bodily inoculation with hands, instruments, cloths, bandage material, etc. Besides, the infective agent is the same, viz., streptococcus pyogenes. The practical result of our study of this question is indeed a very beneficial one; every midwife and physician who has a case of erysipelas in confinement must know that she or he is alone responsible for it, if in charge of the case from the beginning. If nurses or physicians who have treated cases of erysipelas cannot avoid attending to confinements, they must be aware of the danger to their patients, and therefore should disinfect their hands, clothes, etc., as rigidly as possible. We shall discuss these points more in detail in the section on prophylaxis. In all reports of hospital epidemics of erysipelas and puerperal fever we find a ready explanation of the occurrence in contact infection; and that we are right in this explanation is shown by the fact that we know how to avoid such epidemics to-day.

It can be of but little interest to us to follow studies about the occurrence and distribution of erysipelas, the influence of climate, season, weather, etc. It is enough to say that erysipelas can and does occur anywhere on the face of the earth, and at any time. Surely, of just as little importance is the question of race, sex, and constitution.

In regard to the different parts of the body where erysipelas most frequently occurs, Bardeleben says that there are twenty cases of erysipelas of the head to one on other portions of the body. This is easily explained when we remember that, in the first place, the tender skin of the face is most exposed to injuries, and, in the second place, the scalp is the most difficult part of the body to clean. This is doubtless the reason why erysipelas used to be especially dreaded, and of such frequent occurrence, after injuries of the scalp.

Hardly anything remains to be said concerning epidemics and endemics of erysipelas. There is nothing mysterious about them, if we look at them from our point of view. Infection through the air has occurred only in the rarest cases, if ever, while the mode of transportation of the virus is clearly by means of contact; first, by immediate contagion through the hands of a patient suffering with erysipelas, or of those attending him; next, the surroundings of a patient, as clothes, bedding, furniture, carpets, curtains, etc., through contact infection become bearers of the virus, which is through this intermediate link communicated either directly or indirectly to other persons. To avoid endemics in hospitals, it is not only desirable but imperative to have everything prepared to isolate erysipelatous patients entirely, which means to have ready for them

not only an entirely secluded pavilion or ward, but also separate physicians, nurses, etc. Several large modern hospitals, for instance the new Hospital at Hamburg-Eppendorf, have created the position of a so-called septic assistant, who, with his own staff of head nurse and nurses, has entire charge of all septic cases, as of phlegmons, gangrene, erysipelas, etc. All the necessary operations are performed in a special operating-room in the septic ward, and the medical attendant is excluded from assisting at, or witnessing laparotomies. Under these circumstances, with the necessary care, an endemic in such a hospital is next to impossible. Not only this, but the general results of operations are much better, because the assistants are not exposed to infection from poisonous material. (See also the section on Prophylaxis.)

We cannot omit the question of *recurrence* of erysipelas. The experience of a great many physicians and surgeons shows that, in a relatively large number of cases, there is a certain tendency to recur in erysipelas. Most of the text-books mention this same fact, and give all sorts of reasons and explanations for it. While it cannot be denied, *a priori*, that in some cases there is a certain tendency to recurrence, it is a question whether some of the cases reported were not of herpes zoster which had been mistaken for erysipelas. This is an entirely different disease, based on changes in the nerves of the skin, which has absolutely nothing to do with the infectious erysipelas. On the other hand, we have to report that Chantemesse and Sainton came to the conclusion that nervous derangements favor the recurrence of erysipelas. They give as statistics the fact that, out of three hundred and three female erysipelas patients, twelve per cent. suffered from recurrences, partly after catching cold, partly after intense excitement. They prove the perfect connection of erysipelas with the nervous system by the circumstance that erysipelas toxins produce a deep impression on the nervous system. Besides delirium they found erythema, purpura, and arthropyosis, occurring during the disease, also hysterical attacks, disturbances of sensibility, as well as of motility, increased patellar reflex, chorea, and chronic myelitis.

This holds good for cases in which recurrences appear after a comparatively long time. In those cases in which the apparent recurrence is seen within a short time of the first attack, we cannot but find the obvious reason for it in a deposit of streptococci somewhere in the system, especially on the hands, which is excited to activity by some accidental influence from outside, and thus gives the clinical picture of a recurrence, while we really have nothing but a reappearance of the first infection, similar to the exacerbation we observe in the third week of typhoid fever. But, apart from this, some persons show for

a number of years a striking disposition to infection by erysipelas, and they are attacked for five, ten, fifteen years, and longer, once or several times every year. This is called *habitual erysipelas.* Nearly always these patients have some local lesions whence the erysipelas starts; as such we find chronic pustular or ulcerative affections somewhere in the skin, chronic suppuration of glands in scrofulous individuals, chronic eczemas of the face, at the introitus of the nose, on the lips, ulcerous or catarrhal processes in the nose, pharynx, or mouth, affections of the ear, suppurating processes of the tympanic cavity with perforation of the tympanum, affections of the neighborhood of the eyelids or lacrymal sac, varicose veins or varicose ulcers, eczemas of the lower extremities, etc. Moreover, we must not forget that other diseases are frequently mistaken for erysipelas, as, for instance, those erythemata which occur after eating crayfish, crabs, lobsters, fish-liver, mushrooms, strawberries, etc., as well as herpes zoster and gouty eczemas of the skin.

Symptoms.

The clinical picture of the so-called legitimate erysipelas of the skin, without complications, is in typical cases characterized by an acute, rapid rise of temperature, usually up to high degrees, developing simultaneously with erysipelatous inflammation of the skin, and a correspondingly rapid disappearance of the feverish symptoms, with an acute declination to normal temperature or below it, as soon as the local inflammation ceases (see page 412).

The local inflammation is so typical that it is impossible, after having seen it once, to overlook it or to mistake it for something else, in well-developed cases. As mentioned before, it starts from a small lesion in the skin, which may even be healed up at the time the erysipelas is observed. In its immediate neighborhood, we either find red dots, which merge into each other after a short time, or we find one continuous reddened surface. The color varies from brick-red to dark red or livid. The surface of the inflamed part is slightly swollen, and therefore raised above the level of the surrounding skin. The outlines of the affected spot are usually irregular, sometimes tongue-shaped peninsulas projecting quite far beyond the border. One of the typical features is that the boundaries where the redness ceases and the apparently sound skin begins are in most cases very sharply defined. During its progress the inflammation wanders, that is, the disease not only affects new parts by pushing forward its outer boundaries, but the affected spot *in toto* changes its location, the inner frontiers apparently being absorbed, a condition which cannot be better de-

scribed than by comparing it with the way in which spilt alcohol moves along, or in which, borrowing Volkmann's simile, a sheet of paper is devoured by a fire starting at its edge. The erysipelatous reddening is accompanied by a more or less marked doughy swelling, that is, a serous transudation in skin and subcutaneous tissue. The redness disappears on pressure, but reappears again immediately, while the transudation pressed away by the finger cannot come back so quickly, and therefore slight pitting remains. Owing to the increased flow of blood to the infected spot, the latter feels hot to the touch. According to the degree of the swelling, which gives the skin a shiny and more or less tense appearance, the pain is usually tolerable, but increases much on pressure. The greatest transudation is found in the lids, lips, scrotum, penis, labia, and vulva, and then on the ears, toes, fingers, tip of the nose, etc. The serous imbibition of superficial strata of the skin and the rete Malpighii produces not rarely blisters with serous contents, which in the beginning are absolutely clear or yellow, but after a short time may grow turbid and purulent. The blisters usually dry up rather quickly, forming crusts. We then find sometimes, under the latter, superficial suppuration, which only in rare cases of more malignant character progresses towards the deeper tissues; this happens especially if the erysipelas is complicated with phlegmonous symptoms, which are simply another manifestation of the pathogenic action of streptococcus pyogenes.

The explanation of the formation of abscesses is the following: the usual way for propagation of erysipelas being by the lymphatic ducts, we usually see erysipelas spread on the surface; but if the cocci get into the blood, as it has been proven that they do in some cases, the formation of abscesses in the tissues surrounding the primary spot of infection, or even at more or less remote places, cannot be surprising. We must, however, bear in mind that this is not the usual course, but an exception to the rule.

The rapidity with which erysipelatous inflammation spreads is very variable; sometimes it moves within twenty-four hours from half an inch to an inch, sometimes as much as ten inches. In typical, uncomplicated cases, which are by far the most frequent, the inflammatory reddening and swelling undergo a complete *restitutio ad integrum*, without leaving any trace whatsoever of the process which has taken place. Sometimes, however, as before remarked, abscesses are formed even in the deeper layers of tissue.

The general condition of the patient corresponds to the intensity and extent of the local erysipelatous affection. The temperature suddenly, with acute violence, goes up to 104° F. (40° C.) or more, accompanied by one or several chills, and just as quickly sinks again

to the normal, when the affection is over. As long as the erysipelas persists, the temperature at the height of the attack varies mostly between 104° and 106° F. Sometimes, immediately after coming down to the normal, it rises again at once to its former height, which is usually thought to indicate a recurrence, a term which does not quite cover the facts.

The other symptoms are those which usually accompany any high fever or toxic infection. Thus, the regions of the stomach and liver are sensitive to the touch, and there are lack of appetite, nausea and vomiting, great thirst, a furred, dry tongue, headache, prostration, etc. The spleen is often enlarged, the region of the kidneys is not rarely tender to the touch, the urine is mostly dark colored and contains albumin, blood and bile pigment, and micrococci. The quantity of urine is lessened. A fatal result in erysipelas either is due to the general poisoning of the system by ptomains, or ensues because a vital organ, as for instance the cavity of the skull, has been attacked.

Of the highest interest and ultimate value are the experiments conducted by Tuerk, who examined the blood in all infectious diseases, and among them in erysipelas. These hæmatological examinations have nothing to do with the bacteriological contents of the blood or the chemical composition of it, but are confined to the constituents of the blood, the erythrocytes and leucocytes and their respective number, the percentage of hæmoglobin, the number of hæmatoblasts, the quantity of fibrin, and the percentage of the different forms of leucocytes—namely, polynuclear, neutrophile, eosinophile, the large mononuclear, and the small mononuclear leucocytes (also called lymphocytes).

The results of examinations of blood in erysipelas show generally about the same results. Virchow has seen an increase of the white blood corpuscles in this disease, and finds its cause in an acute irritation of the lymphatic system during the attack.

Malassez found that the white blood corpuscles were relatively increased by a decrease of the erythrocytes in uncomplicated erysipelas, and an absolute increase occurs, according to his reports, as soon as erysipelas is complicated by suppuration. The increase then keeps step with the suppuration, and falls as soon as pus is discharged.

Halla found in a pure case of erysipelas of the face a leucocytosis, increasing with the development of the disease (from 12,000 up to 23,000), and at the same time a very perceptible increase of the hæmatoblasts; this latter exists even through convalescence, while the number of leucocytes comes back to normal with the decrease of the temperature. The same results were obtained by Halla in another

case of erysipelas, complicated by pneumonia. He also reports that he found in this case an increase of the fibrin.

Hayem shows that the blood in erysipelas undergoes entirely different inflammatory changes, according to the intensity and extent of the disease. In very light cases, with hardly any fever, he found only a slight increase in the amount of fibrin, and in the number of leucocytes, of which he counted from 7,000 to 8,000. But if the erysipelas is very extended and with high temperature, we find an increase of fibrin and in the number of leucocytes—from 10,000 to 20,-000 or more; the changes of the red blood cells are similar to those in pneumonia. There is a decrease of the number, most to be observed during the crisis, which amounts to from 500,000 to 1,000,000, according to the nature of the case, and a decrease by the stain index, of ten to twenty per cent. during the period of regeneration.

Ehrlich found in two cases of erysipelas a decided leucocytosis, with increase of the neutrophile cells and decrease of the lymphocytes. Limbeck reports having found a slight leucocytosis, which rose and fell with the temperature. A fall in the leucocytosis before one in the temperature may be of value in the prognosis.

Pée observed in five cases a leucocytosis parallel with the extension and intensity of the affection, which ended critically with the fall of the temperature. Reinert found, in the case of a phlegmonous erysipelas of the face (pus under the platysma muscle), a high leucocytosis of 39,600, and a slight decrease of hæmoglobin, as well as in the number of erythrocytes. Epstein found in a case with the same complication as high as 54,900 leucocytes.

Rieder observed six cases, examined during the period of fever, in five of which there was a leucocytosis which never reached any very high degree, with a decided overbalance of the polynuclear elements (ninety-seven per cent.). In one case he found, in spite of high temperatures, normal values, which gave way after defervescence to a leucocythæmia of several days' duration. Zappert found in two cases during the fever normal numbers of leucocytes (5,500 to 6,500). At the same time there was a decrease in the number of eosinophile cells. Klein reports a case in which he found decided leucocytosis, an increased percentage of polynuclear neutrophile cells, a decrease of the lymphocytes, and an absence of eosinophile elements.

Tuerk reports two cases, giving excellent tables which facilitate greatly the comparison and general view. He reaches the following conclusions: Most cases of erysipelas show a slight leucocytosis, while a small number show normal leucocyte values, or slightly below. We cannot draw any conclusion as to the intensity or prognosis of the case, from the absence or existence, or the degree of

leucocytosis alone. Only leucocytosis of a very high degree indicates formation of pus.

Wherever the disease shows any intensity, the polynuclear neutrophile elements outnumber the lymphocytes, while the eosinophiles show a decided decrease, or are lacking entirely. These conditions change again, with the fall of the temperature and convalescence. The mononuclear neutrophile cells are found just as in other infectious diseases.

The erythrocytes usually show no essential changes, except a slight decrease in their number and in the amount of coloring matter. Only after protracted cases a decided chloranæmia seems to occur rather frequently.

Hæmatoblasts and fibrin need not show a change in the very light cases, but are, in most instances, increased in number. The augmentation may reach the very highest degrees, indeed, in the case of the hæmatoblasts.

It is easy to understand that the *duration* of erysipelas cannot be to any extent uniform. There are cases of erysipelas, with no doubt as to the diagnosis, which last twenty-four hours or even less, while others persist for several weeks, with changing intensity and so-called recurrences, sometimes even the same places being invaded and covered again and again by the inflammation. The average duration is from six to eight days, and every case of erysipelas lasting longer than two weeks is, as Billroth says, an exception.

Complications.

Besides the more frequent complications, as formation of abscess, etc., we have to mention others of more or less rarity. Of special interest are those of the eye, which may occur in manifold forms, as, for instance, impairment of acuteness of vision, transient blindness (very rare), panophthalmia with atrophy or suppuration of the bulb —which occurs particularly when an erysipelas of the face attacks the orbital cellular tissues, turbidity of the optic media, iritis, ulcerative processes of the cornea, retinitis, and optic neuritis with atrophy of the optic nerve. Erysipelas of the head is sometimes complicated by catarrhs and suppurative processes of the auditory tract, inflammations and suppurations of the parotid, difficulty in swallowing, and occasionally diphtheritic lesions of the pharynx. The so-called erysipelatous pneumonia must be strictly differentiated from ordinary pneumonia and bronchitis in erysipelas; while the latter, especially bronchitis, are of very common occurrence in severe erysipelas, the so-called erysipelatous or wandering pneumonia is apparently a typical streptococcus infection—still another effect of its virus.

Among the complications observed comparatively most frequently are endocarditis and other diseases of the heart, which mostly end fatally. Since we know that endocarditis can be produced by almost any microbic infection, and since we know that the predominant number of cases of endocarditis is caused by streptococci, it cannot surprise us that some cases of erysipelas are complicated by the latter symptom. Sir Dyce Duckworth reports a number of cases of endocarditis which he has observed as the sequel of erysipelas, though this is comparatively rare. Dr. Hall White reports a number of cases of endocarditis following erysipelas, though he considers them rare. Achalme, quoted by Thoinot, reports that the alterations of the heart are comparatively frequent in erysipelas.

Whittaker in his treatise on diseases of the heart, in Volume IV., of this series, says: "Endocarditis in the course of erysipelas was first noted by Gubler and afterwards was especially studied by Jaccoud and Sulzer. Gendram reported a case of septic endocarditis consecutive to a traumatic erysipelas of the face, and Balana reported a case of endopericarditis in the course of erysipelas of the leg. The streptococcus has been demonstrated in these cases. . . . The streptococcus of erysipelas has been isolated in endocarditis, and from this streptococcus endocarditis has been experimentally produced in animals by Valliard and Vincent, Widal, and Besançon."

If we mention the occurrence of icterus (jaundice), caused by gastric disorders or occurring in its hæmatogenous form in severe cases of erysipelas, and nephritis, which in the worst cases may lead to uræmia, there is nothing left except the very interesting appearance of ulcers in the small intestine, and of transitory hyperæmia of the mucous membrane of the gut, with hemorrhagic diarrhœa.

Erysipelas of the Mucous Membranes.

We have also to discuss briefly erysipelas of the mucous membranes, which undoubtedly occurs, and the course of which is very analogous to that of erysipelas of the skin. The only difference is the great difficulty in the diagnosis of erysipelas of the mucous membranes, which really cannot be made with any certainty until the disease has passed over to the cutis and there shown its typical symptoms, or by bacteriological examination. This difficulty makes it more than probable that a great many of the reported cases had really very little or nothing to do with erysipelas, which has been mistaken for diphtheria, pyæmia, and other acute infectious diseases. The favorite seats of erysipelas of the mucous membranes are the cavity of the mouth, with its adnexa—nose, pharynx, larynx, etc.—the

female genital tract, and the rectum. There are also cases reported in which ulcers in the antrum of Highmore, and in the sphenoid and ethmoid cavities, gave rise to erysipelas, which was recognized as such when it made its appearance upon the skin.

Of the first group, erysipelas of the pharynx with its complications, especially œdema of the glottis, is most to be dreaded. Glottic œdema in erysipelas seems to be usually fatal, in spite of intubation and tracheotomy. An explanation of this can be found only in the fact that the serous infiltration of the mucous and submucous cellular tissue in the region of the epiglottis, aryepiglottic ligament, etc., is transformed into pus, leading to fatal septic and pyæmic symptoms; or fatal cachexia may be caused by extensive suppuration of the larynx itself. Besides this, the usual dangers encountered in diphtheria, such as poisoning by carbonic acid and its consequences, come into consideration along with the general effect of the intoxication.

The second group occurs especially in the puerperium. I have mentioned above the many lesions which delivery brings about, from any of which erysipelas may start. It is, of course, a contact infection, like all the others, a fact which has led modern physicians to avoid internal manual examination, during delivery, as much as possible. All that has been said of erysipelas in other organs might be repeated here, with only slight modifications. The danger of mistaking other infections, especially pyæmia, for erysipelas is very great. There is one point which is characteristic of erysipelas in the puerperium, namely, the possibility of an infection by way of the milk from the mother to the child, streptococci having been found in the milk by myself and others. Another fact to be mentioned is that an erysipelatous infection, starting from the genital tract of the mother, during the last days of pregnancy or even in the beginning of labor, may be transferred *intra uterum* from mother to fœtus by way of the lymphatic ducts.

Diagnosis.

The diagnosis of well-developed erysipelas of the cutis is very easy in typical cases. All the characteristic local symptoms mentioned above, especially the circumscribed redness and swelling of the skin, together with the acute rise of temperature and the course of the disease already described, are so well marked that any one who has seen them once will not fail to recognize them again.

Prognosis.

The prognosis of erysipelas is generally not unfavorable, but, since we have no absolutely reliable means by which to stop the advance of the inflammatory process, we cannot guarantee a favorable result, even in apparently slight cases. The prognosis depends upon a great many circumstances, such as, especially, the location of the affection, its duration and extent, the constitution and age of the patient, the intensity of the fever, etc. The rate of mortality has been very differently reported by different authors, but eleven per cent. seems to be about the right figure, taking into consideration Zülzer's statistics and those of American physicians based upon a large number of cases.

This figure was about right for the time before the treatment by antistreptococcus serum was introduced; while now 3.87 per cent. (taken from four hundred and thirteen cases) is the percentage to which it has been reduced, according to Jackson. (See p. 432.)

Treatment.

In speaking of treatment, we have to discriminate between remedies and curatives. It is only too well known that, in spite of the countless number of remedies in medicine, we possess only a very few curatives for diseases, and most of those, as for instance quinine, were found, one might say, by chance, and their introduction was not based on any theoretical or scientific idea; in fact, these remedies had been discovered and applied long before the causes of the diseases in question were known. It is only within the most recent years that efforts have been made to treat the real cause of the disease and not its symptoms. This, of course, has been possible only since these causes of disease have been found and studied. Of this modern part of treatment, serum therapy, we shall speak later on.

We have to divide the therapy of erysipelas into local, or external, and internal treatment. The object of local treatment in olden times was to influence the part of the body affected with the disease, and to check the spreading of the same. For both purposes, the number of remedies recommended is countless; they vary from the use of the hot flatiron and leeches to the employment of oils, lard, glycerin, chalk, flour, milk, brandy, water, decoctions of lilac, poppy seed, all sorts of salves, the thermocautery, and vesicatories. These remedies were introduced partly as the result of groping in the dark, in the effort to hit by chance upon something which might influence

the disease, or they were remedies which were known by experience to be of value in the treatment of any inflammation.

The local treatment of erysipelas made a decided step forward when, thirty years ago, antiseptics were introduced. As soon as microbes had been discovered to be the real cause of diseases, and the action of antiseptics on microorganisms had been studied, it was only natural to use these preventives in the battle against the infectious agent of erysipelas, though this was not known at the time.

The simplest of external methods, elevation of the affected part, is certainly of some value. In cases of erysipelas of the fingers and scrotum, we can often thus avert gangrene. Various oils, grease, vaseline, and powders in all forms have been applied. Hebra recommended the extensive use of ice, while his followers went so far as to freeze, so to speak, the infected spot. In spite of Hebra's favorable results with this treatment, it is beyond question that gangrene sets in more readily when the vitality of the tissues is thus lowered. The antiseptic remedies were applied partly externally, partly by hypodermic injection. Wet applications of practically every antiseptic solution have been used with varied results, while the subcutaneous injection of carbolic acid and similar antiseptic solutions has been followed by that of such drugs as ergotin, quinine, morphine, and the like.

Hueter, in 1875, recommended early subcutaneous injections of 3 to 5 gm. of a three-per-cent. watery solution of *carbolic acid,* to be made at numerous points into the healthy subcutaneous tissue along the border of the erysipelatous patch. These injections, according to Hueter, need to be repeated only once or twice. Starting from the same theoretical idea which led to the hypodermic injection of carbolic acid, inunction with turpentine was recommended by Luecke and others. Besides this, the use of tar and mercurial ointment has been advocated.

Among other remedies, which are still in use, we have to mention Churchill's tincture of iodine, nitrate of silver, and collodion. Some absolutely reliable authors recommend the *tincture of iodine* strongly, but dwell especially upon the fact that this remedy must be used very energetically. We must not forget, however, that its application is extremely painful, and is absolutely contraindicated in severe cases of erysipelas with a tendency to gangrene and phlegmon.

Nitrate of silver has been employed in different forms, but is applicable only in certain portions of the body. The important point is that the part of the skin to which the remedy is applied should be thoroughly freed from grease, and that not only the reddened portion, but also the adjacent parts, should be thoroughly treated. In 1886, Volkmann had entirely given up the use of solutions of less

than ten-per-cent. strength, and even applied the caustic pencil energetically. His theoretical explanation given for its use was that the nitrate of silver produces an infiltration of small cells in the part surrounding the seat of infection, forming, as it were, a wall of living cells of the greatest vitality, which the erysipelas coccus cannot overcome. How near he came to the truth with these deductions we shall see presently.

Collodion, which was used for quite a long time, seems to have been given up entirely until recently, when Niehans, Sacho, Schneider, and Ratcliffe have recommended it very strongly. Its effect is explained simply by mechanical constriction. Its employment should be avoided on the scalp, whence it is very hard to remove it, and, of course, on the eyelids, where its application is reported to have once caused panophthalmia.

It is needless to mention more fully the use of the thermocautery, as it has been abandoned entirely, but *scarifications* seem to be of the highest value, especially if they are applied in the way which is known as the Kraske-Riedel method. This consists in making incisions somewhat resembling a rail fence, from one and a half to two inches long, forming an enclosure entirely around the affected spot, at a distance of at least one inch, if possible, from the latter. Special attention must be paid that each cut crosses the two adjacent ones, so that the skin on one side is really fenced off from the other. After this has been done, and the wound has bled freely, which is only advantageous, a 1:500 or 1:1,000 corrosive-sublimate solution is rubbed in with some force. Then a wet dressing with the same solution is applied, to be changed every six hours. Of course, this method is limited to the extremities and the trunk. The incisions should not be deeper than just to penetrate the integument, and should not reach the subcutaneous fat. Of all the modes of external treatment which I have used and seen used, the Kraske-Riedel seems to be the most valuable. Special stress must be laid, however, upon operating only in healthy tissue; and this is the more important, as it is well known that the infection commonly progresses farther under the cuticle than the surface inflammation shows. If the fence is too near, we often find that the erysipelas has broken through; that is, it already existed before the operation, in the lower strata of the epidermis, and simply became apparent on the surface the next day. Wherever such a break occurs, it is sufficient to draw a semicircular series of similarly crossed cuts around the new tongue-shaped place, starting and ending at the original enclosure. As to the way in which this operation influences erysipelas, I have more confidence in its power of interrupting the continuity of the skin than in the action of the anti-

septic which is applied afterwards. Although the latter may contribute to the wholesome effect, the severing of the lymphatic ducts, through which the infection chiefly spreads, mechanically stops its progress.

When this method cannot be employed, as for instance in the frequent cases of erysipelas of the head, properly applied *compression* by means of adhesive plaster or a rubber bandage shows good results. If the infection starts, for instance, from the nose, the whole head, in the case of men, is shaved, while in that of women only a circular band of hair, about an inch wide is shaved away. With the hard skull as a base, we have an excellent chance to use compression on the skin threatened by the adjacent erysipelas the spread of which seems to be actually stopped by this method. The theoretical explanation of its action is the same as that of Kraske-Riedel's method, the continuity of a vessel being severed by thorough compression as well as by cutting.

It is easy to understand how the discovery of microorganisms, as the real causes of infectious diseases, should have transformed the therapy so entirely. As soon as they were found, their physiology was studied, as it was to be expected that certain living beings should have certain well-defined conditions under which they live and produce certain secretions. Formerly we could not know how to check the invasion of gaseous, fluid, or other small, supposedly contagious or miasmatic bodies into the human system; we have now to assume that the bacteria enter the body in certain parts, develop under favorable conditions in the part where they entered, and thence spread to other regions.

This fact alone gives us an important explanation of the progress of our therapeutic efforts. Bouchard shows that local therapy acquired a far wider field, so soon as we were able to recognize the signs indicating the first onset of the infection as well as its spread. This gives us the same advantage as that which we derived from Virchow's cellular pathology which took the place of the former humoral and solid pathology. The reason why surgeons could for a long time pride themselves on surer results, impressing even the laity, is to be found in the fact that they applied local methods of treatment. The more internal medicine has turned its attention to the latter, the more positive are the therapeutic results which it has achieved; after a nihilism which reigned for a long while, a celebrated modern physician has said, very truly: "Le vrai médecin, demain, ce sera le chirurgien."

But, in spite of all this, we are, in a great many cases, powerless with the disinfecting agents. While we were led to believe for a while

that we could secure the action of disinfectants by resorption, we have since found that we have to make use of remedies which reside in the body itself, or which develop in the same during certain pathological periods. By this means we can either stop the further development of the bacteria or neutralize their specific toxic effects. One of these remedies is inflammation. Inflammation is one of the most common local effects of any infection. Leber has shown, in a very elaborate treatise on the genesis of inflammation, that it is doubtless true that inflammation is an efficient factor which fights against the foreign invasion and those bodies which are produced in the system under pathological conditions. Especially Metchnikoff has described inflammation as a battle of the organism, with its so-called phagocytes, against a cause of inflammation.

It has to be admitted, however, that irritations which produce, in a certain intensity, inflammation, will be followed in more intense degrees by extensive destruction of tissue, called necrosis. The "appropriate" reaction is thus the result of only mild and moderate degrees of the affection. We have to-day no uniform definition of inflammation; but it is safe to say that the essence of it is the accumulation of leucocytes which most writers regard as a consequence of an exudation from the vessels, as Cohnheim described it. According to the most modern conception, this emigration of the leucocytes from the capillaries and veins is caused by an attraction which the substances of bacterial cells and products of bacterial life exert on them, like other chemical bodies.

The emigration of leucocytes from the blood into the injected focus has, according to Leber's direct observations, the effect of producing a wall around the focus, which hinders the further spreading of bacteria, for instance, mucorinous patches. This same fencing off is effected also by the fibrin produced by the decay of leucocytes or endothelium (Graser), which encloses infectious foci of the peritoneum in a very effective way.

Besides this enclosing effect, the inflammation liquefies the necrotic tissue, and makes it absorbable by the action of the peptonizing ferment. With the elimination of necrotic tissue, the bacteria are also removed from the body.

A third mode of removal of bacteria by inflammation is by phagocytosis, or enclosure of bacteria within the leucocytes, whereby the former are destroyed or carried to other places where they cannot develop because of their small number or poorer nutritive conditions.

Another kind of noxious influence produced by inflammation on the bacteria has been shown by the experiments of Wassermann, Brieger, and Kitasato. The leucocytes which have become massed to-

gether under the influence of bacterial cell substances decay and thus liberate their antitoxins. These unite with proteins of the bacteria, and so produce a specific antidote against the bacteria and their toxins.

Lastly, the exodus of leucocytes is accompanied by the extravasation from the blood of a serous fluid (a lymph rich in albumin) which is directly detrimental to the development of bacteria, either because of the degree of concentration of this fluid, or because of the action of its contained carbonic dioxide or antitoxins, or because of the dilution of the poison. This serous exudation is caused by the alteration of the walls of the vessels, which is a result of the poisoning.

Thus, we find again an explanation why the production of inflammation artificially, in certain cases, is a rational measure. All irritants, as tincture of iodine, porous plaster, and the many derivatives, such as ferrum candens, produce this effect probably in part by creating a general leucocytosis.

Many of the modern authors regard fever as one of the symptoms of infection and inflammation in the same light as Volkmann did; that is, as beneficial to the system. In opposition to Liebermeister, Heubner, and Ziemssen, Strümpell does not admit that antipyretics improve the condition of a patient with fever, but demonstrates rather that the change is for the worse. There are writers who claim that the effect of fever is to eliminate a materies morbi from the body, or, at least, to render it harmless. According to their opinion, this is brought about by the production becoming greater than the loss of heat, and by increased oxidation (more oxygen is absorbed and more carbonic dioxide is passed off); and later by increased disintegration of albumin and elimination of nitrogen, an increased metabolism.

Fever is advantageous because it accelerates the action of the heart and the respiration and increases the exchange of gases, because it gives a greater amœboid activity to the leucocytes (Bakody), and therefore enhances phagocytosis, and because it hinders (Unverricht) the development of certain parasites (pneumococcus).*

Antitoxin Treatment.

The treatment of erysipelas entered an entirely new stage when Marmorek announced, in 1895, that he had succeeded in producing an antistreptococcic serum with which to treat erysipelas and other diseases produced by the action of the streptococcus pyogenes. He

* In the foregoing I have followed closely the admirable treatise, "Lectures on Surgical Infectious Diseases," by T. Th. Kocher and E. Tavel.

took the serum from horses and donkeys, which he immunized with highly virulent cultures of streptococcus pyogenes.

After Marmorek described his antistreptococcus serum, a great many authors took up the question, either repeating his experiments and thus establishing a number of the points which were doubted at first by many, or reporting a larger or smaller number of cases in which they applied the serum in the treatment of human diseases. It is needless to enter into the controversy which followed Marmorek's publication. It may be sufficient to say that it was inevitable that a remedy like this should be found, as it is entirely within the line with Koch's, Brieger's, and Pfeiffer's experiments or theories, and corresponds absolutely with our modern conception of diseases, their causes, and their cure. Although we have learned not to expect too much from any serum treatment after the experience with Koch's tuberculin, it is safe to say that the antitoxin treatment has gone beyond the experimental stage, and has shown such definite results in the hands of so many reliable investigators that we are really entitled to hope to see it employed generally.

The list of authors on this subject is too large to give in full. It may be sufficient to mention only a few of the names to show how eagerly the question has been taken up. H. Richardière described (1895) a case of erysipelas of the face, treated with Marmorek's serum, cured in a few days. Several days later an exanthem was observed, somewhat similar to erythema and purpura. In 1896, cases were also reported by Bolognesi, and Bovet and Huchard compared the results of the former methods of treatments of erysipelas with those of serum therapy. Then Michel, Parascandolo, Pane, Sciandone, and Pertat contributed to this question. Stewart reported a case of the streptococcus antitoxin treatment of recurrent erysipelatous lymphangitis, while Tison wrote on the application of this antitoxin not only in the treatment of erysipelas, but also in that of puerperal fever, furunculosis, and scarlatina. In 1897 Lemoine reported on Marmorek's serum, chiefly in regard to his experiments with it on animals, while Normanding related his clinical experiences, and Parascandolo reported another series of cases, treated with Marmorek's serum. Others are Eschweiler, Schenck, Monti, Magill, the Vienna correspondent of *The Lancet*, two publications by Courmont, Sabrazes, and Rondot. The latter reported rapid improvement of the general condition and reduction of the temperature; the swelling went down quickly, the course of the disease was decidedly shortened, and the changes of the skin underwent a complete *restitutio ad integrum.* Of all these authors, we find only one, Bolognesi, who, after trying serum treatment, had reason to be dissatisfied with it. He came to

the conclusion that mild cases healed without application of the serum, and that therefore the latter was unnecessary; and even severer cases had been seen to undergo complete reparation, therefore he could not see the value of the serum. Gouin reports a case of erysipelas of the face in which the injection of 2 c.c. of Marmorek's serum made the temperature, as well as the rapidity of the pulse, go down within twenty-four hours, while the erysipelatous dermatitis decreased decidedly. After two injections the erysipelas had vanished. Calvo also reports cases. Jackson reports 413 cases of erysipelas treated with antitoxin, of which 3.87 per cent. died, instead of 5 to 12 per cent., which is the estimated percentage of death in erysipelas according to different authors. His conclusions are that the serum lowers the temperature, reduces the local inflammation, and improves the general condition.

Bonome and Viola repeated the interesting experiments of Smirnow, D'Arsova, and Charrin on the influence of electricity on cultures of pathogenic microbes. They selected for their experiments the streptococcus pyogenes, the cultures of which they treated with intermittent currents of high tension. The cultures had a virulence which killed a rabbit with a dosage of one five-hundredth to one eight-hundredth in about four days. The electrical currents used were created by the Tesla transformer, which was fed by a Ruhmkorff's inductor in connection with accumulators. The cultures used in the experiments were kept in U-shaped tubes, in which platinum wire electrodes were immersed. The electricity was turned on each time for from twenty to forty minutes. The authors came to the following conclusions:

1. Electrical intermittent currents, of high tension, possess the faculty of rendering harmless the most virulent cultures of streptococcus pyogenes without changing the chemical reaction or form of the parasites. This effect is produced even after a short action of the currents, and is constant.

2. The effect takes place only with toxins in solution; the streptococcus transfused into a new nutritive medium develops with the same activity as before, and keeps its pathogenic quality unchanged. It can be kept viable in electrified cultures for two weeks.

3. The toxins of the streptococcus are transformed under the influence of these currents into antitoxins, which show an analogy to the antitoxins of the blood serum in immunized animals.

4. The streptococcus antitoxins obtained by electricity from *old* cultures are very active. It is possible to neutralize *in vitro* streptococcus cultures of tenfold the lethal dose for rabbits; but the antitoxins obtained in the same way from *fresh* cultures are weak, because they

contain only a small quantity of toxin to be transformed into antitoxin.

5. These antitoxins possess a strong protective and curative property against streptococcus infection in rabbits.

6. They have the character of real vaccines, and may, like the vaccines, be obtained after Mironoff's method by heating the culture up to 55° to 60° C.; but this is not without danger to the system of the rabbit, as it produces progressive marasmus and rise of temperature in the beginning.

7. The effect of these antitoxins is probably caused by the incitation to form substances which are able to destroy the streptococcus. *In vitro*, this effect is shown by the destruction of the streptococcus.

As a final proof of the identity of the different streptococci found in diseases of man, we have to mention results of bacteriological experiments following up streptococcal infections. The different human diseases in which chain cocci are found very often intermingle and are connected genetically. True erysipelas develops in direct connection with a primary focus of suppuration (Petruschky). On the other hand, there are suppurative processes which are derived directly from a primary erysipelas (Knorr, Petruschky). Erysipelas may be followed by sepsis (Pfuhl). Otitis media caused by streptococci may be followed by streptococcal septicæmia, with suppuration of the joints (Wetter). As has long been known, local puerperal infections may terminate in septicæmia.

We might assume, in those cases in which an existing streptococcus infection is followed by another different one, that, pathologically as well as chemically, a new infection has taken place. Two very strong reasons are against this assumption: first, the cases mentioned are too frequent; second, the streptococci of the primary focus and those of the disease and in connection with it show constantly the same degree of virulence. Therefore it is beyond any doubt that the same causative agents produce suppuration starting from an erysipelas, and also sepsis starting from the suppuration of erysipelas.

Toxins.—There cannot be any doubt that the chain cocci produce toxins which cause fever, general symptoms, and death, but the chemical nature of these toxins and their isolation from cultures have been studied only lately. It is not certain yet whether they are products of the secretion of the cocci or are the contents of the bacterial cells.

Immunity.—A number of authors—Knorr, Marmorek, and others—have succeeded in immunizing certain animals. Marmorek reports that he has rendered animals poison-proof against very large doses of his most virulent culture, by treating them (a lamb, a donkey, and a horse) with highly virulent living streptococcus cultures. With the

serum of these animals he was able to protect rabbits against infection with living virulent streptococci. Afterwards he employed this serum in the treatment of man. He treated, as early as 1895, forty-six erysipelas patients, all of whom were cured. He used as a beginning dosage 10 c.c. of serum of horses and donkeys which had been immunized with very virulent streptococcus cultures. The immunization was achieved by the subcutaneous injection of small doses of highly virulent streptococcus cultures (not toxins), which were increased and repeated as soon as the animal had recovered. He later reported four hundred and thirteen cases of erysipelas which he had treated with his "sérum antistreptococcique."

Prophylaxis.

The best way to treat erysipelas is doubtless to prevent it. It is really the most important thing we have gained in our studies of disease of late that, the real source of infectious diseases having been found, we are enabled to check the spread of the disease and to prevent the infection in a great many cases with almost absolute certainty.

In hospitals especially the strictest prophylaxis against erysipelas is necessary. The most simple and effective way of preventing the introduction and spread of erysipelas in the hospital is to refuse admission to erysipelatous patients. Though this seems unnecessary hardship, every surgeon is fully justified in insisting upon the rule, as otherwise he risks the lives of all his operated patients for the treatment of one. A great many hospitals, therefore, follow this rule. Other and more fortunate hospitals have a special septic division, which is a small hospital in itself, situated on remote grounds, completely isolated from the rest of the building, and having no connection with it. The special medical assistant, head-nurse and nurses, cook, and other help, are not allowed to enter the main hospital.

In those cases in which it is impossible for the physician to refuse treatment to a patient with erysipelas, he must be fully aware of his responsibility and the grave danger to which he exposes all his other patients; but untiring vigilance and the most minute cleanliness will go far toward obviating the risks. First of all, a great deal can be done in treating a patient without touching the most infectious parts with the hands, but only with instruments; the latter must be sterilized every time, and form the outfit for the treatment of this patient alone—not to be used in any other case; then, the rubber gloves, to be had now almost anywhere, are surely one of the most effective means of protecting the hands of the surgeon from becoming infected while treating septic cases. Even the rubber gloves can

easily be sterilized by steam under pressure without being affected at all, and if worn during the entire procedure of handling, dressing the patient, and so on, and then left at the patient's place, they are of the highest value in keeping the physician's hands unaffected, and thus preventing infection of other patients. Besides this a physician treating a patient with erysipelas should always put on an operating-gown covering his clothes completely. This is to be left at the patient's house and to be sterilized there. I might mention here, though it seems trivial, that a very simple and at the same time efficient way to sterilize the clothes of a physician treating patients with an infectious disease, is to have the suit pressed. This is better done at home, in order not to spread the infection. A number of bacteriological experiments which I have carried on for a while have convinced me that this method is quite sufficient for all practical purposes. Nevertheless, the personal responsibility of the physician is very great, and what used to be unfortunate complications, which nobody could foresee or prevent, now come very near being the result of criminal negligence on the part of the medical attendant.

One of the most important, and at the same time interesting, chapters of any treatise on erysipelas would be the description of the influence of erysipelas or erysipelas toxins on malignant tumors; but this will be treated of in another volume of the work, and the reader is therefore referred to that volume (XVII.).

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SIMPLE CONTINUED FEVER.

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SIMPLE CONTINUED FEVER.

Synonyms.—Ephemeral fever, Febricula, Irritative fever, Ptomainic fever, Gastric fever, Catarrhal fever, Mucoid fever, Abortive fever, Sun fever, Nervous fever, Mountain fever, Synocha, Accidental fever, Idiopathic fever, Non-Specific fever.

General Description.

It is more satisfactory to the purposes of this article to give a general description of this fever than to bind ourselves down to a close definition. No fixed and fast term can be formulated to convey a complete idea of it. Some authors do not even undertake its discussion. And yet the physician cannot be long in practice before he encounters cases which cannot be satisfactorily classed among either the inflammatory or the specific fevers. He then learns that there is a non-contagious, not apparently infectious, rarely epidemic febrile condition, having no definitely recognized etiology or pathology, which continues variably from two or three to twelve or fifteen days—seldom longer—which is rarely fatal, and which, for want of more precise information, must be recognized as *simple continued fever*. When this condition lasts only two or three days, it is spoken of as *ephemeral fever*. When its duration is prolonged to several days, while yet the fever remains mild, it is ordinarily referred to as a *febricula* (diminutive of *febris*). When the fever exceeds this limitation and continues ten or twelve days or longer, it constitutes the *protracted simple continued fever* of authors in general.

Other terms applied to this fever refer to the cause—supposed or real—or to the circumstances which surround the patient. Thus, some speak of an *abortive fever* when simply a mild continued fever occurs in a patient during the prevalence of some specific infectious disease, while no sign or symptom of the epidemic disease manifests itself other than the rise of temperature, the malaise, the headache, etc., which usually attend the febrile stage. Many such cases may be abortive forms of typhoid fever, it is true; but there occurs none of the other characteristic signs or symptoms of the graver trouble to confirm the diagnosis.

Again, we hear of *catarrhal fever*, which may be attributed to the vaguely understood condition of "catching cold." Or, because of the amount of mucus coughed or hawked up, or mixed with the alvine discharges, or perhaps found as a deposit in the urine, the accompanying fever has been called *mucoid fever*. This rare condition, however, has moderate recognizable pathological lesions which ordinarily distinguish it from simple continued fever in the strictness of definition.

Still others speak of a type of *gastric fever* as one of the forms of simple continued fever, which is often traceable to an imprudence in diet. Such imprudence, acting as an irritant, has called for the name *irritative fever*. Some of these cases, if exact causes could be traced, might undoubtedly be classed among *ptomainic fevers;* indeed, in a general sense, such a term is not inappropriately applied to some obscure cases.

Workmen who have become exhausted by overwork, while exposed to tropical sun-heat for long portions of the hot summer day, oftentimes develop a fever of several days' duration without other ostensible effect, which has been designated as *sun fever*. Such cases are usually included under the heading of simple continued fever—although some of them might be the better studied under the general classification of insolation.

Prolonged mental strain, especially when accompanied by depressing anxieties, sometimes so acts as to induce a febrile condition, which has been styled *nervous fever*. Such a condition is most often noticeable in the strongly impressionable.

Synonyms enough have been used, and forms enough of simple continued fever have been referred to, which find confirmation in the rounds of any experienced physician, to show that there is a febrile condition affecting the human race which cannot be classed among the acute infections—however much in certain particulars it may resemble a specific infection.

Etiology.

From what has been said, it is evident that simple continued fever has many causes, and yet is without a well-defined specific one. It is without a *distinctive* microorganism or ptomain or toxin as a causative element, although any of several appears at times to produce it. It may, therefore, be spoken of as a symptomatic fever.

Many clinical facts, as well as physiological observations, point to the existence of thermogenic centres in the spinal cord and base of the brain. These centres control those metabolic processes in the tissues which result in heat production. It seems to be the drift of

opinion that pyrogenic elements, resulting from a microorganism or a ptomain or a toxin in the circulation, act primarily upon these thermogenic centres so as to produce fever, and "secondarily, upon the tissues, through perversion of nutritive elements of the blood, to cause degenerative changes." Hence the action of such pyrogenic elements may be noted as *hæmic causes.*

There are also *nervous causes* which mechanically affect "some portion of the nervous system unassociated with inflammatory changes." Thus, "both direct and reflex irritation of the nervous centres are known to produce rise of temperature without coincident inflammation" (Loomis, "Practical Medicine," 1895).

Of the numerous conditions which act causatively in producing this fever, none perhaps is so constant as that almost indefinable one known as "*catching cold.*" From time immemorial, it has been recognized that prolonged exposure to a lowering temperature in a breeze or in a draught of air—especially if laden with moisture—or to dry air blowing upon a portion of the body that is moist with perspiration, are important factors in the process of "catching cold." The *pars minoris resistentiæ* receives the most pronounced effect. "The sensory nerves are thrown into a peculiar state which is propagated to the nerve centres, and reflected by them along certain other channels that are endowed with special susceptibility to this form of stimulus. Should the affected tract be sensory, we get rheumatic pains or neuralgia; should the vasomotor centre be implicated, alterations in the calibre of the blood-vessels may result (as proved by numerous experiments)—especially vascular dilatation (hyperæmia) in particular areas; inflammatory processes may be attributed to a transfer of the stimulus to the trophic nerves, . . .; lastly, should the heat-regulating centre be involved and its activity depressed, fever may result. . . . The state of excitement induced in the cutaneous nerves by cooling of the surface must be *sui generis;* for irritation of the skin by chemical agents, wounds, and inflammatory processes does not give rise to phenomena of a like kind." For a fuller discussion of "how we catch cold," the reader is referred to Seitz's article in Ziemssen's "Cyclopædia of the Practice of Medicine," Vol. XVI., which is not impaired by its age of over twenty-one years.

There can be no question as to the *hysterical origin* of a number of cases of simple continued fever, occurring mostly in females. In the experience of every busy general practitioner, there are cases marked by a moderate, though irregular, elevation of temperature which continues for several days, with headache more or less severe, and an irregular amount of nausea, without other apparent cause than that which is usually recognized as hysteria.

Digestive disorders of various kinds often induce an attack of simple continued fever. Ferments—either gastric or intestinal, developed from improper food in cases of functionally impaired stomach or bowels—are frequent causative factors. A very common cause is development in the alimentary canal of the powerful poison, tyrotoxicon. The eating of tainted foods has frequently caused the fever.

Keating has noted "a tendency to hyperpyrexia manifested by cases of febrile conditions observed at *high altitudes.*" And Work groups the majority of cases of so-called *mountain fever* under the head of simple continued fever.

Clinical experience shows that some people have febricula from apparently trifling causes—due to idiosyncrasy. The inhalation of noxious vapors, as of sewer gas, or the emanations from putrescent organic matter may be enumerated as causes. The writer has seen it produced more than once from neglect in keeping clean the plate of artificial teeth worn by a patient.

Fatigue, excitement, depression of spirits, as by grief, exposure to sun heat, the stay of some weeks of the non-acclimated in tropical climates, etc., are also causes of this fever. It is altogether probable that the continued feverish condition, lasting a week or more, due to heat, to nervous causes, to overwork, etc., may be attributable to the action of leucomains being formed more rapidly than they are excreted.

It would scarcely be more than a play upon words to undertake to speak more at length of the causes of those forms of simple continued fever which are termed "irritative," or "catarrhal," or "gastric," or "sun fever," etc. Such terms, while they do not explain the *modus operandi* of the cause in producing the fever, indicate in a general way its nature. But in the vast majority of cases it seems impossible to trace the fever to its prime cause. In fact, we must admit ignorance as to the precise manner in which poison elements in the blood excite those metabolic processes which are productive of fever.

From what has been said, it is plain that we may expect this simple continued fever to occur in either sex, at all ages of life, during any season of the year, in any climate, and in all sections of the civilized world. It is said to be more common in children and during adolescence than in the more advanced periods of life. It is probably more prevalent in tropical sections than in the colder climates—not referring to mountain temperatures. But it has not been possible to secure statistics with reference to any of the points referred to. There is no evidence to show that this fever is either contagious or epidemic. In fact the occurrence of an epidemic, or a history of apparent contagiousness would at once lead us to suspect the presence of

some infectious disease which the febricula was simulating or concealing.

One attack of this fever confers no immunity against subsequent attacks.

Pathology.

No definite pathology has been established for simple continued fever. We naturally expect to find that morbid condition of organ or of tissue—more or less defined—which is incident to the cause of the disease—if, indeed, that cause is discoverable. In those cases traceable to disorders of digestion—gastric or intestinal—there may be evidence of a mild catarrhal gastroenterocolitis. Possibly other cases may present those putrefactive changes, or cerebral venous engorgement, or liver and kidney parenchymatous changes, etc., suggestive of insolation. Probably a few cases may present some microscopical changes in the pons, or in the nerves emanating from it, or in some portion of the ganglionic cells; but all such pathology is conjectural. It is not improbable that some cases would suggest the mildest forms of cerebrospinal meningitis. No definite alteration has been found in the composition of the blood, even though there may have been reason in supposing the case to have been an abortive form of an infectious disease, as influenza, typhoid fever, etc. Even cases presumably of ptomainic origin have not been proven pathologically nor bacteriologically or chemically to be such. Enlargement of the spleen or liver is not outlined by inspection, palpation, or percussion. Urea and uric acid—as in acute fevers and inflammations in general—are eliminated in the urine in increased quantities until the crisis of the fever is reached. In short, all the changes recognized in the tissues and fluids of the body as occurring in this disease are inconstant and possess rather the proofs of irritation than of distinctive inflammation.

The fact is that simple continued fever, without complications, is so rarely, if ever, fatal that opportunities have been wanting for a satisfactory pathological study. Until such opportunities arise we must remain content with what now must be confessed to be purely conjectural pathology.

Symptomatology.

Simple continued fever cannot be said to have a definite period of *incubation*. It may develop in a few hours, without prodromes, after a dietary indiscretion or after an imprudent exposure of person to moisture or draughts of air, or it may follow worrying mental strain when nervous tire is evident. Again, its invasion may begin at a

time corresponding in length to the recognized period of incubation of the acute specific infection that may be prevailing in a community. In short, there is no evidence by sign or symptom that the so-called "idiopathic fever" has a fixed period of incubation.

The *invasion* is generally sudden. A varying degree of lassitude may have been noticed for a short while, or there may have been a dull headache for a day or so or a part of a day, when a very positive sense of chilliness or even a decided rigor may usher in the attack. In an hour or two more the thermometer indicates a rather rapid rise of temperature, which, in twenty-four hours or less, may run up to 103° or even to 105° F. Even higher temperature degrees have been noted. Respirations and pulse beats will have correspondingly increased in frequency. A vague, dull headache, mostly frontal, or at times a more intense headache, with throbbing of the temples, sets in and continues throughout the attack. Discomfort or actual pain is felt in the muscles of the back. The joints—the larger ones especially—are oftentimes sore and stiff and feel as if they needed lubrication. Anorexia and great thirst are to be expected. Nausea and even vomiting may occur—the more to be looked for if there have recently been errors in diet. The tongue bears a whitish or a white-yellow fur. The tonsils are occasionally reddened and swollen, but sordes does not collect about the teeth. The bowels are costive, especially so in those forms of synocha which are not traceable to intestinal ferments or irritants. While the pulse is rapid, full, and tense and the skin hot and dry, the secretion of urine is scant and febrile. Urea, uric acid, and the urates are freely eliminated in the urine, which, on cooling, deposits its salts, giving rise to lateritious sediment. The face, of course, is flushed. Labial herpes is common, and non-characteristic eruptions, such as erythematous flushing or a scarlet rash, are frequent accompaniments of the fever. Sudamina upon the abdomen often appear; and Musser says that "pale bluish maculæ are sometimes seen."

In the "synochal variety" of this fever, so much spoken of by the practitioners of the eighteenth century, convulsions not infrequently marked its invasion, especially in children. In adults, delirium is common enough. This severe form of simple continued fever is now rarely seen except in the tropics.

The characteristic of this disease is fever—pure and simple. When the *ephemeral form* presents itself (which is by far the most common variety in the temperate zone), the ushering-in signs and symptoms are the most pronounced. The temperature reaches its maximum in less than twenty-four hours as a rule, observes a fastigium of scarcely another twenty-four hours, and then rapidly falls to

normal, the defervescence being usually marked by free sweating, perhaps a diarrhœal tendency, and generally copious urination.

In the *febricular* and *protracted continued forms*, the invasion is by no means always so well marked. Chilliness is common, and the temperature rises much more rapidly than in typical typhoid fever and attains its fastigium (about 103° F.) by the end of the third day. This elevation of temperature, with moderate after-midnight remissions, is usually quite evenly maintained for a varying period of from five or six to twelve or fifteen days; then there is, as a rule, termination by crisis. During the entire attack there is generally nothing in the signs or symptoms beyond the continued fever to occasion alarm or anxiety as to the prognosis. Emaciation is not so marked as in typhoid fever of equal duration; and the "getting-up" is much more rapid than after this latter disease, so that under judicious tonic after-treatment the patient may be restored to his or her normal health in a week or so.

Immediate *recurrence* of this fever is very rare; although, as already said, one attack does not give immunity against a subsequent one after full recovery.

Sequelæ.

There are practically none except such as may be induced by the grossest disregard of the laws of hygiene.

Prognosis.

This is exceedingly favorable, unless a grave complication of extraneous origin—so far as simple continued fever is concerned—sets in as an intercurrent disease. It is so rarely fatal that but few opportunities for autopsies have presented themselves.

Diagnosis.

At times nothing is more difficult than to make a satisfactory diagnosis of simple continued fever. In truth, it is often not made until after the termination of the disease, when the patient has returned to his accustomed rounds of duty or of pleasure. Previous history, uranalysis, and bacteriology furnish us only negative helps. It is not improbable that some cases of febricula are abortive forms of the infectious disease that may be prevailing at the time. Some degree of immunity as to such prevailing infection may so modify the true disease as to alter its every symptom and thus leave us with the clinical history of simple continued fever alone. During epidemics of smallpox, for instance, it is not unusual for the physician and other

attendants—themselves thoroughly protected by vaccination against even the eruption of varioloid—to become sickened and have so-called "nurse's fever."

In looking for points of diagnosis of simple continued fever, it must be conceded that we are considering a condition of variable etiology, pathology, and symptomatology. But it is not improbable that, in the progress of time, what must now be regarded as a clinical entity will be divided into a number of well-defined febrile ailments. In the present stage of our knowledge, we may recognize how a micro-organism of some kind may be introduced into the system, and may appreciate, as a natural result, the development of fever; but it is hard to explain why the fever continues in some cases after the toxins have apparently been swept out without notable change being left in the blood or tissues. We can only suppose that there is a varying susceptibility of the nervous system in different individuals. For instance, in one person heat stroke may affect the subject as if he were the victim of apoplexy; another person is so influenced by the same cause as to suffer from feebleness of the heart's action, etc. In other cases, however, the same cause apparently produces the condition recognized as simple continued fever. Why these different effects of the same cause in different individuals, we are at a loss to understand. Until some of the positive sciences, such as chemistry, microscopy, bacteriology, etc., come to our help we have to deal with the fever under consideration only from a clinical standpoint.

Typhoid fever is the disease with which simple continued fever is most usually confounded. But in the latter disease the temperature reaches its acme by the second or third day, and its defervescence is more abrupt than is the case in typical typhoid fever. Besides, in the disease under consideration, the characteristic typhoid eruptions on the body are absent; there is no characteristic tenderness in the right ileocæcal region, no pea-green alvine discharges; meteorism is usually absent; the tongue is not often fissured, and seldom is there a collection of sordes about the teeth and gums; the spleen is not materially enlarged; Eberth's bacillus is not found by bacteriologists, nor does the blood respond to Widal's test. The diazo-reaction test is too uncertain under any circumstances to be depended upon alone as a diagnostic proof of typhoid fever. It thus appears that simple continued fever is told from typhoid fever, which it most resembles, by the absence of the characteristics of the latter. Yet we must confess that we cannot always be certain whether or not some unrecognized atypical form of typhoid has not been present.

Typhus fever is more easily eliminated from the question. The early marked prostration and the brain symptoms and the early re-

semblance of the rash to that of measles, as well as the frequent complications of bronchopneumonia and post-febrile paralysis, etc., readily exclude simple continued fever.

Erysipelas and *acute rheumatism* cannot be mistaken for the disease under consideration, although some writers have referred to their similarity in the earliest stages. Rheumatic fever without arthritis generally develops endocarditis, which does not result from simple continued fever.

Malarial fevers cause marked enlargements of the spleen and are due to malarial organisms which are usually easily detectable on examination of a drop of blood.

Typhomalarial fever is a term which will not down, notwithstanding the most persistent effort of certain authors. Without discussing the *pros* and *cons*, the writer is satisfied that there is a disease, in this section of the country at least, to which the term is applicable. Leaving out of consideration the points which diagnose it from distinctively typhoid fever and malarial fever, it resembles simple continued fever in the persistence of a fever, the absence of abdominal symptoms and eruptions of typhoid fever, and the negative results of *repeated* blood examinations as to response to Widal's and other tests on the one hand, or as to the finding of malarial parasites on the other. Nor is there definite response to the so-called "therapeutic test of quinine" in either. The spleen is not perceptibly enlarged in either of the two conditions. Fatal termination of either is very rare, and convalescence from both is rapid. We know of no distinctive diagnostic marks between these two conditions unless it be that the so-called *typhomalarial fever* is a disease of usually about three weeks' duration and its decline is more gradual than is that of simple continued fever.

If simple continued fever develops during a prevalence of *scarlet fever* in a community, the former would be told from the latter disease by the absence of the scarlatinal eruption, nor is there the characteristic sore throat, and there is no swelling at the angles of the lower jaw.

Gastric and gastroenteric catarrh have a more gradual development usually from an easily recognized cause, and the fever also develops more gradually.

From so-called *worm fever* simple continued fever is told by its more regular run of fever, by the absence of the marked nervous perturbations, and the peculiar foulness of breath which are common in worm fever. In simple continued fever the upper lip has not the thick, swollen look of worm fever, nor is the appetite voracious. Sometimes the therapeutic test of a suitable anthelmintic may be required.

From *continued thermic fever* simple continued fever may be recognized by the history of the case. Heat fever begins generally as a hyperpyrexia with pinpoint pupils. Unconsciousness, with a clammy cyanotic surface of the body is common.

During the prevalence of an exanthematous infection it is prudent, in doubtful cases, to withhold announcement of diagnosis for a day or two, when one or more of the characteristics of one or the other disease will manifest themselves.

Treatment.

If we are fortunate in discovering the cause of the fever in a given case, treatment, of course, must be directed to its elimination and then to combating its effects. Many instances of ephemeral fever have thus been prevented from running into protracted simple continued fever. Nearly all of such cases are benefited by an initial purgative dose of calomel and soda, followed in a few hours by a saline cathartic. Magnesium sulphate and Seidlitz powders are useful for the purpose indicated. The writer, however, prefers "cream-of-tartar lemonade" —simply lemonade, in which about two levelled teaspoonfuls of potassium bitartrate, dissolved in a little hot water, has been added. This is a palatable, refreshing, and refrigerating draught, and is a good diuretic eliminant as also cathartic. If objection should be urged against the use of calomel, consecutive doses of fluid extract of cascara sagrada—either alone or in combination with aromatics—may be substituted. During the early days of the fever it is better to secure two or three bowel actions a day than to have one action in two or three days.

Hydrotherapy is of undoubted advantage in the treatment of this fever. Comfort and benefit are alike secured by cool-water sponging. High enemata of *cool* water afford perhaps the surest means of quick reduction of pyrexia. It is not required that the water used shall be uncomfortably cold to the patient. Instead of pure water some practitioners use decinormal saline solution. From six to ten ounces or more may be used every three or four hours. This acts as an antiseptic solution, is readily absorbed by the lacteals, supplies an element of nutrition to the system, and serves as a refrigerant or cooling mixture, thus reducing the febrile temperature in the interior of the body without the risk of shock or other injury. The good effects extend to the surface and brighten the feelings as also the appearance of the patient.

In a few hours after the initial cathartic dose is given the steady use of small doses of phenacetin, salol, and powdered digitalis in

combination may be begun with advantage in relieving pains and aches and also reducing fever temperature to about normal. Some modification of the following to suit individual needs is the usual prescription of the writer:

℞ Phenacetin, ...	ʒ i. (4.0)
Salol, ...	℈ ij. (2.6)
Powdered digitalis, ...	gr. vi. (0.4)

M. Make twenty capsules. S. One every three or four hours, lengthening the intervals as the symptoms improve.

Tincture of aconite—from a quarter drop to a full drop—especially in combination with from five to ten drops of spirit of nitrous ether, given with a little water, is a favorite with many physicians.

This line of prescription, with rest in bed and a simple liquid diet, will most quickly and safely tide the patient over into speedy convalescence.

RELAPSING FEVER.

BY

LEO POPOFF,

ST. PETERSBURG.

RELAPSING FEVER.

Synonyms.—Typhus recurrens, Febris recurrens; *German*, Rückfallstyphus, Rückfallsfieber; *French*, Typhus à rechutes; Fièvre à rechutes; *Russian*, Vozvratnaïa goriachka, Vozvratnaïa likhoradka; *English*, Recurrent fever.

Definition.—Relapsing fever is a contagious, febrile disease, characterized by its cyclic course, to which it owes its name, and by the presence in the blood of a specific microorganism known as Spirochæta Obermeieri. In accordance with the present state of our knowledge of this subject and with the ideas now prevailing in the scientific world, we must include under this term also the morbid affection described formerly by Griesinger under the name of "bilious typhoid." This author himself regarded bilious typhoid merely as a variety of relapsing fever, and was the first to adopt this view. Nevertheless he deemed it advisable to describe the affection as a disease apart and under a special name, as a wholly autonomous morbid entity. The consequence of this was that many authors who wrote concerning bilious typhoid after Griesinger, of whom we need mention only Lebert, agreed with him as regards the autonomy of this disease in relation to relapsing fever. The explanation of this confusion is probably to be found in the fact that into the description of bilious typhoid, given by Griesinger, there entered certain elements referable to analogous morbid processes, to which this name was equally applicable and was indeed applied by some writers, although the processes were actually entirely different from those of recurrent fever. A confusion of this sort was moreover possible and even natural at a time when Obermeier's spirochætæ had not been discovered and when affections presenting so great an analogy with relapsing fever were relatively little known. At the present time, however, the certain knowledge which we have acquired concerning the relations between these microorganisms and relapsing fever on the one hand, and of the diseases which resemble the latter on the other, enables us to differentiate these morbid processes with great precision, and to give to them in our descriptions the place which belongs to them.

History.

There is no doubt that the disease known at the present time under the name of recurrent or relapsing fever existed, just as some other typhoidal affections, for a long time before it was recognized by clinicians as a morbid entity or was so described by them. Some writers (Spittal, Diamantropoulos) incline to the belief that relapsing fever existed at the time of Hippocrates, basing their opinion upon certain indications relative to this affection given by Hippocrates in his description of epidemics which had prevailed on the island of Thasos near the coast of Thrace. But other writers, of whom some are of high authority (such as Hirsch), do not regard this opinion as founded upon sufficient evidence.

The first more or less definite historical facts which we have on the subject of relapsing fever are found in the writings of English, or rather Irish and Scotch, authors, and as a rule go no further back than the first half of the eighteenth century. In the description given by Strother of the epidemic of fever which raged in London in 1729, we find the fact mentioned that many of the patients suffered relapses. The same fact is noted in the report by Lind of the contagious fevers met with in the navy. But the first more exact description of this affection and one embracing the characteristic symptoms of typhus recurrens was made by Rutty, who had studied the disease during the epidemic which prevailed in Dublin from 1739 to 1741.

At the same time (1741) appeared the first mention of the disease in Scotland. Similar observations of the simultaneous appearance of epidemics in Ireland and Scotland were noted also towards the end of the last century and in the early years of the present one (1799–1800, 1801, 1817–19, and 1826–27). During all these years relapsing fever occurred frequently, usually also at the same time as typhus fever, a fact which explains why several authors regarded these two typhoidal affections as simply two different forms of the same disease. Christison, following the opinion generally held at his time, even maintained that relapsing fever might engender typhus fever. The epidemics above mentioned were followed by a long series of great epidemics prevailing in the forties of the present century (1841, 1842–43, and 1846–48) in Ireland, Scotland, and England, which furnished us with many valuable observations and made possible a more profound study of the disease. Among the numerous authors who described the epidemics of that period we must mention particularly Barker and Cheyne (1801, 1816–21), O'Brien and Graves (1826),

Cormack, Craigie, Henderson, Steel (1843–44), and many others whose works greatly advanced our knowledge concerning this malady. As a result of their labors relapsing fever, which up to that time had been confounded with relapses of typhus fever or of typhoid fever, was finally recognized as an entirely independent disease and received the name which it has preserved up to our own day.

Recurrent fever often presented itself during these epidemics, especially in Ireland and Scotland, under such a malignant form and was so frequently complicated with icterus that in some cases it was mistaken for yellow fever (Graves, O'Brien).

Among the English writers who did much to enlighten us concerning the specific nature of relapsing fever we may mention, in addition to those referred to above, Jenner and Murchison. The former (1850) brought out very clearly and precisely the most important peculiarities and even the most characteristic symptoms of this affection, and established upon a firm basis the differential diagnosis of the disease. Murchison, in his classical work on "The Continued Fevers of Great Britain" (1862), has given us a very detailed and complete description of relapsing fever, and has in so doing contributed very largely to our better knowledge of the disease. It was always Ireland which, in the great epidemics that prevailed in the United Kingdom in 1868 and 1873 and also previous to this date, remained the centre whence the disease spread throughout Great Britain. It was Ireland again which was the source whence this scourge passed beyond the British Isles and invaded other parts of the world, such as America. To this we shall return later.

Next to Great Britain, Russia occupies the first place among European countries as regards the date of the appearance and the extent of prevalence of relapsing fever. It was unknown there, however, until nearly one hundred years after it had been recognized in England. In 1833 the disease appeared in Odessa. In the winter of 1840–41 it prevailed extensively in Moscow, where it was frequently observed under the grave icteric form. In 1857–58 recurrent fever raged in eastern Siberia, and in the port of New Archangel in Sitka. In 1863 it appeared again in Odessa, and in 1864 invaded St. Petersburg and the neighboring provinces. In 1865 it began to spread more widely and was reported in various cities and provinces of Russia, and since that time it has invaded nearly every part of the country, from Siberia and Turkestan (1865–66) to Poland (1866–68), and from Finland (1865) to the Caucasus (1865). In many places relapsing fever has appeared several times in quick succession, attaining almost the proportions of a considerable epidemic.

During the Russo-Turkish war of 1877–78 relapsing fever, together

with typhus fever and malaria, spread widely among the troops operating in Asia Minor and in Bulgaria. But while in Asia Minor the morbidity of typhus fever and that of relapsing fever were almost equal, in Bulgaria relapsing fever prevailed to a much greater extent than typhus. During the period immediately following the campaign, from 1877 to 1888 and even later, relapsing fever appeared frequently in various parts of the empire, especially in the great centres of population. As regards St. Petersburg, where the affection has become almost endemic since 1864, several years (1881, 1882–83, 1886, 1890–91–92, and 1895–96) are particularly to be noted as years in which the disease assumed the proportions of a true epidemic.

The epidemics observed in Russia have, equally with those in Great Britain and Ireland, contributed greatly to the increase of our knowledge concerning the nature and symptoms of relapsing fever. Keyman, Pelikan, and Levestamm have given us good descriptions of the Moscow epidemic in 1840–41. Later we find excellent accounts of the epidemics of 1863–64 and the following years given by Bernstein, Botkin, Hermann, Zorn, and others. The epidemics subsequent to these gave opportunity for the noteworthy researches of Heidenreich, Motchoutkovsky, Albrecht, Metchnikoff, and others, who have studied in detail many of the special features of this morbid process, and who have in particular rendered important service in the study of the specific microbe of the disease, discovered in Germany by Obermeier, and of its relation to relapsing fever.

Of the continental countries Germany comes next to Russia in respect of the prevalence of relapsing fever. The disease appeared for the first time in epidemic form, concurrently with typhus fever, in 1847–48 in the northern part of Germany (at Königsberg in Upper Silesia) during a famine—a coincidence which had previously been observed in Ireland. It was, however, especially in 1868–69 and later, in 1871–72 and 1878–79, that this disease, which had, as it was supposed, been imported from Poland, assumed its greatest development. Very grave cases were observed in Breslau, Posen, and Berlin.*

The disease was noted in 1879–80 in the south and west of Germany, the Rhine provinces, Heidelberg, and Bavaria. In Austria epidemics have occurred in 1847, 1865–66, and 1877–78, chiefly in Galicia and Bohemia, although Engel saw a case of relapsing fever in Bukowina as early as 1846.

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* As bearing upon the history of relapsing fever in Germany it is interesting to note that M. D. Lapchinsky says that we find a description in the work of Spitz of a disease which prevailed epidemically in Minden in 1771–72, and which was characterized very distinctly by the peculiar symptoms and recurrent attacks of relapsing fever.

German observers have recorded epidemics of relapsing fever (rather frequently the bilious form), occurring simultaneously with cases of typhus fever, at Cairo in Egypt. It is very probable also that the epidemic described by Larrey was one of the bilious forms of recurrent fever. In his classical work on the infectious diseases, Griesinger has given us an excellent description of relapsing fever, in which he includes the affection which he calls "bilious typhoid," although he also describes an affection under the name just given as a distinct morbid entity. This work of Griesinger was instrumental in adding greatly to the knowledge of relapsing fever, not in Germany only, but among physicians of all countries. Among other German writers deserving of mention are Lebert and his pupils, Wyss, Bock, and others. Following these come Litten, Ponfick, and others who have contributed valuable studies on the epidemiology, symptomatology, and pathological anatomy of typhus recurrens.

But without doubt the most important contribution to the study of this disease which has been made in Germany is the discovery by Obermeier, in 1873, of spirochætæ in the blood of patients suffering from relapsing fever, the organisms being found during the attack of the fever and disappearing in the apyretic interval. This discovery was not only of considerable importance in the study of the disease in question, but it also contributed greatly to our knowledge of the pathogenesis of infectious diseases in general.

The discovery of Obermeier was followed, not in Germany alone but in other countries as well, by a long series of researches in the same direction. We have already mentioned the Russian authors who worked in this field and who obtained important results. Among the Germans who have added to our knowledge of the bacteriology of relapsing fever we may refer particularly to Litten, Birch-Hirschfeld, R. Koch, Engel, Weigert, and others.

Of other countries in Europe in which epidemics of relapsing fever have been observed we may mention the Scandinavian peninsula, where slight visitations were recorded in 1851, 1861, and 1865. It is supposed that the infection was imported in these years from Finland.

France has never had to suffer from epidemics of relapsing fever. Several cases were, indeed, observed in Val de Grâco following the Crimean campaign, but there were never enough cases to constitute a real epidemic. Small collections of cases were also noted towards the end of 1866 and the beginning of 1867 (Morache). In Belgium and Holland also only small isolated epidemics of relapsing fever were noted in 1859 and 1867. Switzerland, Italy, and Spain have never been visited by relapsing fever.

Greece, Dalmatia, Turkey, and Asia Minor, as well as many of

the islands of the Mediterranean (Malta, Cyprus, and the Ionian Islands), have often been invaded by relapsing fever in its most malignant form (bilious typhoid). The same is also true of Egypt and of parts of Algeria and Abyssinia. Tholozan saw many cases of relapsing fever among the troops returning from the Crimea and among the patients in the hospitals at Constantinople. In these countries the affection was often taken for yellow fever or for malarial fever, and was sometimes called by the local names given to malarial fever, such as Bukowina fever, Levant fever, Smyrna fever, etc.

In India relapsing fever has been known since 1855–56, epidemics having been recorded in 1859, 1863–64, 1868, and subsequently. From India the disease was carried to the islands of Mauritius and Réunion. In China it was observed by European physicians in 1865–66.

Coming to America, and especially the United States, we find that relapsing fever was imported into Philadelphia by Irish immigrants in 1844. In 1847 it was similarly observed in New York, whence this same and subsequent years it spread to neighboring towns. The affection was limited in its progress to the States on the Atlantic coast, and it never assumed the proportions of a large epidemic, although there were numerous cases of malignant form among the colored inhabitants. In 1850 Flint saw cases of the disease at Buffalo, and in 1869–70 the disease again appeared in Philadelphia among immigrants, and was carried thence during the two following years to other parts of Pennsylvania. At the same time it occurred again in New York, but always among the Irish immigrants. According to Wells the disease, during the summer of 1870, which was extraordinarily hot, assumed the character of a true epidemic, there being no less than five thousand cases, of which two hundred terminated in death, the fatal cases occurring especially among the Irish and the negroes.*

We have no data concerning the prevalence of relapsing fever in Central and South America.

From the sketch which we have just given it is seen that relapsing fever does not act in the same way, as regards its development, in all countries. In some it reigns endemically, with frequent epidemic exacerbations, while in others it occurs only sporadically, and any

* From the account given by Hirsch, we must conclude that the epidemics which prevailed in America, especially in Philadelphia in 1821 and in North Carolina in 1829, affecting chiefly the negroes, were epidemics of relapsing fever (bilious form). This acquires greater probability from the fact that the negroes are more or less immune to yellow fever, which is the disease to which these reports are more commonly assumed to have referred.

epidemics which may arise tend to disappear spontaneously. Other countries again seem to be wholly immune to the disease, there being no tendency at any time to the occurrence of an epidemic spread, even after the introduction of isolated cases.

Etiology and Bacteriology.

At the beginning of this work I stated that relapsing fever is a contagious disease which occurs ordinarily in epidemic form. Since the celebrated discovery by Obermeier in 1873 of spirochætæ in the blood of patients with relapsing fever, the contagious principle of the disease has been referred to these microorganisms, which we shall describe below. That which constitutes the most demonstrative and convincing proof of the relation of these microorganisms to the disease in question is the truly characteristic fact of their presence in the blood of sufferers from the disease during the febrile paroxysm and their absence during the period of apyrexia. Numerous researches undertaken by various investigators (Engel, Weigert, Litten, Birch-Hirschfeld, Koch, Carter, Minkh, Heidenreich, Motchoutkovsky, and others) since the announcement of Obermeier's discovery have shown without any question that, on the one hand there is no relapsing fever without the presence of spirochætæ, and on the other hand these microorganisms are always encountered in the blood of patients suffering from this disease. Riess alone claims to have observed a large number of cases of relapsing fever in which he was unable to find any spirochætæ in the blood.

In the great majority of cases we find the spirochætæ in the blood only immediately before, and especially during, the febrile paroxysm. Heidenreich, however, has noted their appearance in the blood several hours or even one day before the beginning of the paroxysm, and Carter has seen them as long as one or two days before. The rule is, however, as we have stated it above, namely, that the microorganisms do not appear until just at the beginning, or at the most a few hours before the beginning, of the febrile paroxysm.

But as soon as the paroxysm begins to subside and the crisis approaches the spirochætæ lose their mobility and disappear from the blood. This disappearance is noted especially at the period when the critical sweat occurs. It is only in exceptional cases that the presence of the spirochætæ has been noted in the blood during the apyretic period. Bliesener found them some hours after the critical defervescence (the thermometer marking 36.1° C. or 96.5° F.), Birch-Hirschfeld during the first two days of the first apyretic period, and Winzer even on the third day after the fall of tempera-

ture. In a case of relapsing fever complicated with pneumonia, Naunyn found the spirochætæ continuously present in the blood for a period of two weeks, but he observed that their number after the fall of temperature was much less than it had been during the height of the disease.

A new febrile access is characterized by a reappearance of the microorganisms in the blood.

We do not ordinarily find spirochætæ in the blood of persons who have died of relapsing fever (Orth, Ponfick). Lachmann found them in six cases, and Heidenreich also in a case which had ended fatally during the height of the pyrexia. In one of Lachmann's cases there was a considerable increase in the number of the parasites after death. Ordinarily, when the spirochætæ are found after death they are enclosed in the spleen (Lyoubimoff, Metchnikoff).

As regards the relative number of spirochætæ in the blood in the different stages of the disease, we find the following figures given by Motchoutkovsky: During the first day of the attack (from eight to fourteen hours after its beginning) they are present in small number, and at a given magnification we find only one in ten to twenty fields. During the succeeding days their number increases progressively so that by the second day we find one microorganism in every three or four fields. Twenty hours or so before the appearance of the sweats the number of parasites is at its maximum, that is to say, about twelve in every microscopical field. From this moment the number begins to decrease, and within about half an hour after the commencement of the period of sweating the microbes have completely disappeared from the blood. The same progressive increase and decrease in number are observed during the periods of relapse. The greatest recorded number of spirochætæ, twenty to thirty in each visual field, was observed in a case of Motchoutkovsky during the third paroxysm. The number may be found to vary during the same paroxysm, even without any change in temperature, if the observations are made at sufficiently brief intervals. It is not impossible that this may be due to the production of several generations of the microorganisms during the same paroxysm, and in this case the variation in number would be explained by the coincidence of the moment of blood examination with the appearance of a new generation or the destruction of the old one. Another fact which argues in favor of a rapid multiplication of the spirochætæ is that related by Albrecht. In a preparation of blood, in which at the beginning only three spirochætæ were counted in the field, a very much larger number was found six hours later. The greatest care is, however, necessary in formulating conclusions from such facts, for we know that the same preparation may contain

varying proportions of microorganisms in its various parts, and also that different preparations of blood drawn at the same time from different portions of the body may contain varying numbers of spirochætæ (Motchoutkovsky).

As to what is due the disappearance of the spirochætæ from the blood at the period of crisis and what becomes of these microorganisms upon their disappearance, we at present know but little. The following fact is of great importance in this regard. The spirochætæ, which disappear from the blood of the patient within a few hours after the crisis, or even sooner, will outside of the organism live and retain their mobility for a long time in blood kept at the ordinary temperature (thirty-seven days according to Motchoutkovsky, but only fourteen days according to Heidenreich). We know also that upon losing their mobility the microorganisms degenerate, becoming gradually granular. Müllendorf, preserving the spirochætæ outside of the body in a fine capillary tube, found them alive at the end of eight to ten days. After this time they became disintegrated into very minute granules. The same disintegration of the organisms was observed by Pasternatsky, who exposed them to the action of elevated temperature in hermetically sealed tubes. Mamourovsky has found that the spirochætæ change their shape ten to twenty hours before the end of the febrile paroxysm. Little by little their spiral filaments straighten out into threads which are perfectly even or preserve only traces of the spiral form. At the same time their protoplasm, which up to that time was perfectly homogeneous, becomes granular in places, a change which is observed with great clearness in preparations stained with fuchsin. The spirochætæ then present themselves under the form of chains of spirals or filaments, an appearance due evidently to the fact of an unequal degeneration of the protoplasm. Those portions which have lost their vitality lose their property of fixing staining reagents. The number of these spirochætæ in chains increases towards the end of the febrile paroxysm.

Metchnikoff was never able to observe the destruction of the spirochætæ in the blood of monkeys, although he repeated his examinations every five or ten minutes. He believes that the function of destroying these microorganisms belongs especially to the spleen, the elements of which (phagocytes) absorb them, while the elements of the blood as well as those of the other organs, such as the liver, the bone-marrow, etc., do not possess this power.

It is, however, interesting to note that we do not find the spirochætæ, during the crisis, in any of the secretions or excretions (sweat, saliva, urine, milk) or in the fæces, or in the vesicles of

sudamina or herpes, or in the serum of blisters. And as a rule, also, they are not found in the blood of cadavers.

In opposition to all other experimenters, N. Ivanoff concludes that phagocytosis in the circulating blood constitutes a phenomenon necessary in every case and in every paroxysm, occurring either naturally in man or experimentally in animals. He examined the blood of a relapsing-fever patient a few hours before death, after having stained it after a modified Roux's method, and also examined in the same way the blood of monkeys experimentally inoculated with the germs of relapsing fever. He found microorganisms in all stages of their destruction by the white blood corpuscles, beginning with those which were but little changed and could be distinguished from the free spirochætæ only by their fainter stain, and ending with those which were completely destroyed and consisted only of masses of granular detritus.

The experiments of Gabritchevsky demonstrated that there appear at certain determinate periods in the blood of patients with relapsing fever substances endowed with very pronounced bactericidal properties as regards the spirochætæ. If we add to blood containing the spirochætæ some blood taken from one who has just emerged from a paroxysm of relapsing fever, we shall see, in a period of from one-half to one hour at a temperature of 37° C., or in from two to four hours at ordinary room temperature, all the spirochætæ become immobile, change form, and die. If instead of adding serum from a person in the apyretic stage of relapsing fever we add normal blood serum, the spirochætæ will live for from two to four days. The duration of life of spirochætæ taken from the blood of a patient and preserved outside of the body is shorter the nearer the time of taking the blood is to the termination of the febrile paroxysm. It follows evidently from this that the bactericidal property of the blood increases in proportion as the febrile paroxysm progresses and attains its maximum towards the beginning of the crisis.

It is difficult, in the present state of our knowledge, to explain satisfactorily the granular appearance of the spirochætæ which Mamourovsky observed towards the end of the paroxysm, as well as that which Pasternatsky and Albrecht noted in certain other conditions. We have no sufficient grounds for regarding this as sporulation. It is more probable that we are here in the presence of a phenomenon of organic degeneration, or disintegration, and of death. However this may be, it appears to be difficult at present to explain the disappearance of the spirochætæ from the blood by phagocytosis alone and especially by splenic phagocytosis, as Metchnikoff would have us believe. Many facts which we shall cite below, as well as the experiments of Gabritchevsky to which we have just referred and those of

Ivanoff, speak in favor of some entirely different causes for the disappearance, that is to say, the destruction of the spirochætæ in the blood of persons suffering from relapsing fever. Ivanoff inoculated with blood taken from a patient with relapsing fever some monkeys, among which were some which had previously received an injection under the skin of blood taken from a person who had just passed through an attack of this disease. While the control animals suffered within a few days from the characteristic symptoms of relapsing fever, those which had received the preventive inoculation escaped with a fever of moderate duration unaccompanied by the presence of spirochætæ in the blood.

It may be regarded as an established fact that there is a very definite relation not only between the parasitic elements and the morbid process observed in man, but also between the liquid which contains these parasites (such as the blood of a patient) and a similar pathological process observed in animals, and this fact puts beyond all possibility of doubt the existence of a pathogenic relation between the spirochætæ and relapsing fever. For this reason we think it will not be superfluous to give here a more detailed account of the parasite of relapsing fever as well as a description of the measures employed in the examination to determine its presence.

Morphology of Obermeier's Spirochætæ.

The parasite of relapsing fever belongs to the class designated spirobacteria or spirobacilli, by which we understand microorganisms having the form of mobile rods curved for the most part in the shape of a corkscrew. The spirobacteria are divided into spirilla and spirochætæ. The spirilla, called also vibriones, are characterized by longer spiroid turns and are endowed with lively vibratory movement. Among them we find the Spirillum serpens, Sp. undula, Sp. rugula, Sp. tenues, Sp. rotulans, and the comma bacillus of Asiatic cholera. Most of these microorganisms form spores. The spirochætæ resemble the spirilla, but differ from them chiefly in that for the most part they are longer and finer, and have shorter and closer spiral turns. In this class we have the Spirochæta plicatilis, found in stagnant water, Sp. buccalis seu denticola, found in the buccal and nasal mucus, and finally Sp. Obermeieri, with which we have here to deal. By reason of confusion in nomenclature then prevalent, this microorganism was formerly called by various names, such as spirothrix, protomycetum recurrentis, or spirillum recurrentis. Most commonly it was called simply spirillum, a name which it has preserved even to the present day.

The examination of the blood for spirochætæ is made as follows: After having washed with alcohol and water or with soap or with a weak (1 : 2,000) solution of corrosive sublimate the skin on the palmar surface of the third phalanx of a finger or, preferably, that of the lobule of the ear, a small puncture is made by means of an ordinary needle, which has been previously sterilized in the flame of a lamp. As soon as one or two drops (sufficient for an ordinary examination) have been collected in this way on a glass plate they are immediately protected by cover-glasses. If a larger quantity of blood is needed we may resort to a simple incision with a bistoury, to wet-cupping, or even to a venesection, according to the amount required. We may study the spirochætæ in either the living or the dead state. In the first case the blood is examined directly on an object glass or in a cell under the microscope. In the second case we employ dried preparations stained by any of the reagents mentioned below.

The best staining method for the recognition of this organism is that of Günther, which was employed before him by Albrecht. Dried preparations of blood are subjected for ten seconds to the action of a five-per-cent. solution of acetic acid in order to extract the hæmoglobin from the red blood corpuscles. The acid is then neutralized by exposure for several seconds to the fumes of ammonia, and the microorganisms are finally stained by immersion of the preparation for ten minutes in a saturated aqueous solution of aniline gentian violet (Ehrlich-Weigert method). The spirochætæ may also be very well stained in the ordinary solution of carbol-fuchsin diluted with water, or with a one-per-cent. solution of formaldehyde in sufficient quantity to cause the solution to become perfectly clear and to take on a reddish color. They also stain very satisfactorily in a mixture of two to four parts of this solution of fuchsin (Ziehl) with twenty to twenty-five parts of Roux's stain, proposed by this investigator as a stain for the Loeffler bacillus, diluted with three or four parts of water (Ivanoff). Seyliger recommends the following method for staining spirochætæ contained in the blood (natural or defibrinated): To one drop of blood on the object-glass is added one drop of a weak solution (1 : 1,000) of methylene blue, and the cover-glass is then put on, its edges being sealed with paraffin in case it is desired to preserve the preparation. Most of the spirochætæ will be stained within two minutes and almost all of them by the end of five minutes. The threads of fibrin and the blood corpuscles do not take the stain, the nuclei only of the leucocytes being colored, but much less intensely than the spirochætæ. The latter preserve their mobility for some minutes after being stained. Koch has succeeded in staining the microorganisms in the tissues by means of aniline browns (vesuvin,

Bismarck brown), and Hueppe and several others have obtained good results in these cases by the employment of methylene blue and other basic aniline colors. The spirochætæ cannot be stained by Gram's method.

When we examine a drop of blood freshly drawn from a person suffering from relapsing fever, we observe first of all, according to Obermeier and others, a movement in mass of the blood which seems as if produced by a light shaking of the red blood corpuscles. It is

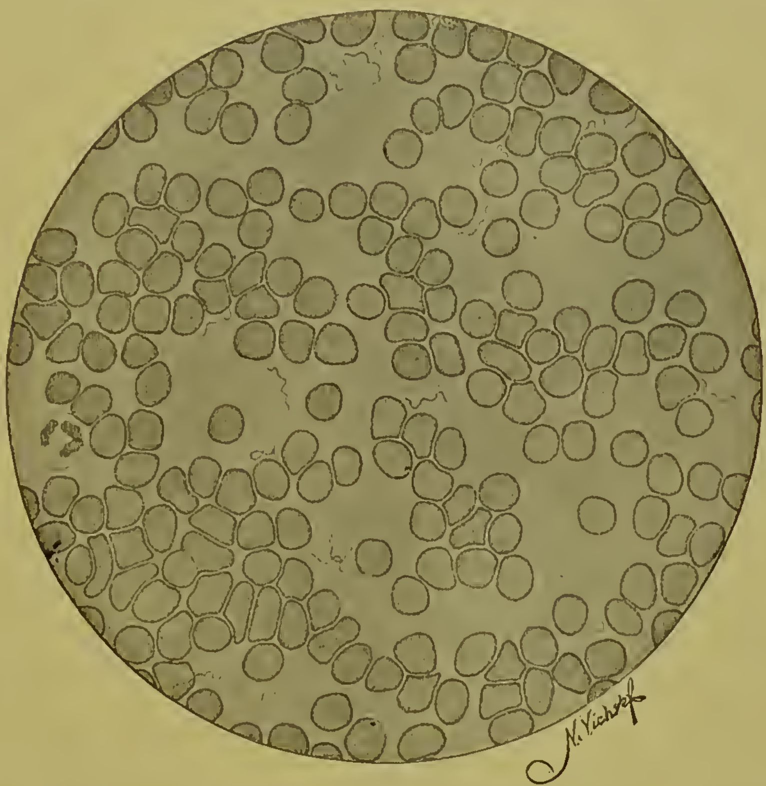

FIG. 23.—Blood from a Patient with Relapsing Fever, Showing the Spirochætæ. From a dried preparation stained with carbol-fuchsin. Between the groups of red blood cells, and sometimes adherent by one extremity to a cell, are seen the spirochætæ, sometimes isolated, sometimes joined together to form loops. × 560.

not difficult, however, to persuade ourselves, upon more careful examination and under a higher magnifying power, that these movements are caused by the spirochætæ themselves. Among the red globules, sometimes isolated and sometimes nummulated, move with great rapidity very fine, delicate corkscrew-curved filaments of varying lengths with feeble refractive properties. These filaments are observed either swimming freely in the serum or attached by one extremity to one of the blood corpuscles. In consequence of their extreme tenuity it is not always perfectly easy to detect these filaments. At the beginning we see ordinarily only a part of a spiro-

chæta which is noticed under the form of a vibrating fibril or of a small filament having very lively movements. Gradually this filament becomes more and more distinct and seems to increase in length. The microorganisms may be detected under a magnifying power of 350 to 400 diameters, but ordinarily much greater magnifications are employed in this study. In the venous blood the spirochætæ swim for the most part in the serum near the surface so long as they are alive and mobile. The dead organisms fall to the bottom.

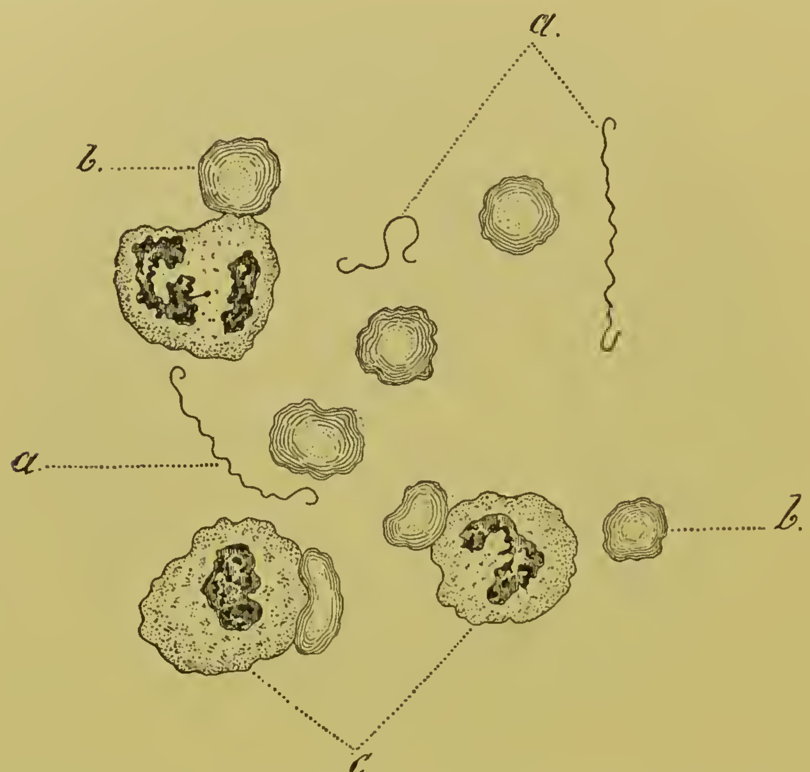

Fig. 24.—Blood from a Patient with Relapsing Fever. From a dried preparation stained with gentian violet. *a*, Spirochætæ; *b*, erythrocytes; *c*, leucocytes. × 1050.

Examined separately each spirochæta is seen to be a fibril of extremely small diameter, resembling as regards size a very minute fibrin thread. Its protoplasmic mass is brilliant, homogeneous, and of a soft consistence. The length of the microorganisms is not constant, varying according to the approximation or separation of the individual spirals. Obermeier estimated their length as equal to the diameter of from one to six erythrocytes, that is to say, from 10 to 30μ; Heidenreich's estimate is 42μ; and other observers give still higher figures. We must not forget, however, that the spirochætæ sometimes form chains by joining their extremities (Fig. 3) and so may increase very considerably their apparent length. No one has ever seen any

parts or structure of any kind in these organisms, except the granular degeneration which obtains under certain conditions and to which we have adverted above. Tiktin alone has recently claimed to have seen very fine colorless transverse striæ, visible under a magnification of 1,200 diameters, or more rarely under one of 700 diameters. The number of striæ observed by him was from two to three. Sometimes, according to the same observer, the spirochætæ present the appearance of a chain composed of many very fine links.

The spirochætæ are perfectly colorless, but have well-marked outlines which become more distinct when the organisms have lost their mobility. At this time the transverse diameter increases somewhat, except at the extremities which taper off to a point. The number of spirals varies from six to sixteen according to the length of the organism, and their radius from a quarter to a half of the diameter of a red blood cell. The spirals do not lie in the same plane, but resemble a corkscrew. This spiral form disposes the microorganisms to entanglement, and when once they have become bound together they do not separate, notwithstanding their movements, but form, when present in considerable numbers, little balls or thick felt-like layers. Engel says that by altering the focus we may clearly distinguish the helices or corkscrew-like turns of the spirochætæ. According to Heidenreich the spiral form is most easily observed when the spirochætæ begin to move slightly and when the longitudinal axis of a filament becomes perpendicular to the field of observation. Under such condition we see only the upper extremity or a cross-section which appears sometimes under the form of a small circle constantly turning more or less eccentrically, or sometimes that of a cone narrowing from above downwards, or a small cylinder having a similar rotary movement.

The movements of the spirochætæ are in general very varied, and we distinguish several kinds: 1. A rotary movement around a vertical axis; this movement, which is very active and constant, is the most characteristic; some writers call it an undulatory or zigzag movement. It is produced by a very strong spiral rotation of the microorganism around its vertical axis, forward or backward. In connection with this movement, which is always exceedingly active, we observe a great flexibility of the spirochætæ by means of which they can avoid or turn around any obstacle which they encounter in their path. 2. A movement of progression, either forward or backward. This movement may be very active or it may be slow. 3. Lateral movements of flexion and extension or pendulum movements. Some writers mention also other forms of movement, tetanic, elongation, and retraction, etc.

These active movements of the spirochætæ are attributed to the existence of cilia, which are, we must admit, extremely difficult of detection with our present instruments. These cilia have, however, been seen on spirilla by some investigators (Koch, Karlinsky). Their existence has also been demonstrated by means of photography.

The movements of the spirochætæ are most active when the blood has been taken at the height of the febrile paroxysm. During the first day the movements are still rather slow, but their rapidity increases, reaching its highest point at the acme, and then decreases towards the end of this stage. As the period of the critical sweats approaches

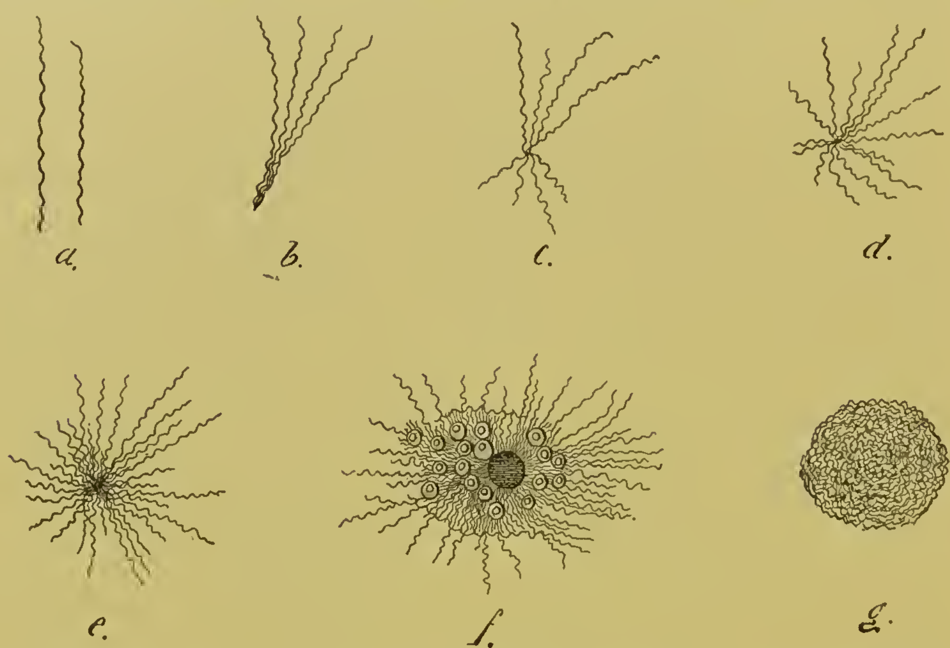

FIG. 25.—Spirochætæ in the Blood. *a*, Several filaments joined laterally and giving the appearance of a single thick filament; *b*, several filaments joined at one extremity and along a part of their length and then diverging in brush shape at the other extremity; *c*, *d*, *e*, little stars or knots of various sizes and forms; *f*, a large knot in which are entangled several red blood cells and one leucocyte; this entire mass, as well as all the others here pictured, were endowed in the first specimen with a rapid vibratory movement; *g*, a ball of dead spirochætæ. (After Heidenreich).

we find that many of them have already become motionless, while others have only very feeble movements. At this time they often become curved on their axis. Finally the spirochætæ disappear completely so that during the sweating stage they are nowhere to be found in the blood.

The microorganisms are found in the blood either completely isolated or united in twos or greater numbers. When agglomerated they have the appearance of moving together as one mass. Sometimes we may observe vast quantities of these microorganisms forming masses or balls resembling amœbæ; from this mass of protoplasm extend free extremities, and the whole is endowed with a lively move-

ment. Sometimes these masses have the appearance of felt, and often they take on star shapes. In their interior they may hold imprisoned red blood cells which they move about by means of their prolongations. The presence of massed spirochætæ is a sign of interference with the circulation, that is to say, of blood stasis. In proportion as the blood in the preparation under study becomes cool the movements of the spirochætæ become slower and finally cease altogether. Certain of them become massed together in a finely granular substance, probably albuminous in character, or are enclosed in a fibrinous network.

It is very interesting to know how the spirochætæ act in different media under the influence of various reagents, and also at varying temperatures. Studies in this direction have been made principally by Heidenreich, Motchoutkovsky, Engel, Weigert, and more recently also by Seyliger.

As regards the influence of temperature, it has been found that the spirochætæ live, that is to say, preserve their movements longest, in blood outside of the body at the temperature of the room (according to Heidenreich, for fourteen days at a temperature of from 18° to 21° C.—65° to 71° F.), but lose their movements quite rapidly at higher or lower temperatures. At moderate febrile temperatures, up to 38° C. (100.4° F.), they become motionless in fifteen hours; at 41° to 41.7° C. (105.8° to 107° F.), in four hours; at 44.5° to 46° C. (112.1° to 114.8° F.), in two hours and a quarter; and at 48° C. (118.6° F.), in half an hour. Spirochætæ which have become immobile under the influence of a febrile temperature will sometimes recover their power of movement some hours after the reduction of this temperature. The reduction of the temperature below that of the room will also hasten the period of suspension of movements. Thus at a temperature of from 2.5° to 3.6° C. (36.5° to 38.5° F.) the movements cease in two days and half, and at one of −5° to −6° C. (23° to 19.2° F.) they cease in two hours. It is a remarkable fact, however, that after a reduction of the temperature to −10° C. (14° F.) the spirochætæ recover their movements after the blood has thawed and has been raised to the ordinary room temperature.

If oxygen is passed through the blood the spirochætæ become immobile in from thirty minutes to an hour and a half. In an atmosphere containing a large proportion of carbon dioxide their movements are speedily arrested. The addition of plain water in the proportion of one part to four parts of blood causes the movements of the spirochætæ to become slower and to cease ten times more quickly than in undiluted serum. If water be added in larger proportion the spirochætæ perish very rapidly. A solution (one-half to one per

cent.) of sodium chloride is, according to Engel, as favorable to the life of the spirochætæ as is serum, but according to Motchoutkovsky the microorganisms live only three-quarters as long in this solution as in serum. A two-per-cent. solution of sodium chloride destroys the spirochætæ almost instantaneously. The addition of one part of chemically pure glycerin to twelve parts of blood causes a suspension of movements of the microorganisms in from two to three hours; one part to eight arrests them almost immediately; but one part to twenty prodnces almost no effect. The addition of sodium carbonate in the proportion of two parts per cent. begins to exert an inhibitory effect upon the movements of the spirochætæ in four hours, and stronger solutions act still more energetically. Sugar in a two-per-cent. solution produces no marked effects, but a solution of five-per-cent. strength arrests the movements of the microorganisms instantaneously. A five-per-cent. solution of albnmin has no action, one of twelve per cent. stops movement at once.

Spirochætæ preserve their mobility the greatest length of time (from thirty to one hundred and thirty days) when contained in the medium which is natural to them, that is the blood, kept from the air and at ordinary temperatures, as we have already stated; but it is only necessary to add the blood of another individual, whether healthy or ill (septicæmia, dysentery), in order to shorten quite perceptibly (by several days) the life of the organisms. The addition of blood taken from the cadaver of one who has died from relapsing fever during the febrile paroxysm arrests the movements within from two to four hours. We shall speak below of the effects produced by the addition of blood taken from another patient suffering from relapsing fever.

Saliva in the proportion of one part to four parts of blood arrests the movements in from one to four hours. A one-per-cent. solution of hydrochloric acid arrests the movements. Sweat, added in the proportion of one part to four, arrests the movements in two honrs. Human milk, in the proportion of one part to four, arrests the movements of the spirochætæ in from five to six hours, bnt cow's milk, added in the same proportion, arrests them in one hour. Bile, taken from a cadaver eighteen to twenty-six hours after death, arrests the movements when added in quantity greater than that of the blood; the thicker the bile is the more quickly it acts. The urine of a healthy man, added in the proportion of one to four, slows the movements very perceptibly, and the same is trne of the urine of a patient suffering from relapsing fever.

Salicylic acid arrests the movements of the spirochætæ when it is added in the proportion of one part to five hnndred; sodinm salicylate acts more feebly and the addition of one part to six hundred

has no apparent effect. Creosote in aqueous solution of the strength of six-tenths per cent. destroys the spirochætæ in two or three minutes, and the same is true of potassium permanganate in one-half of one-per-cent. solution, and of potassium iodide in one one-hundredth of one-per-cent. solution; the latter in five one-hundredths of one-per-cent. solution kills the microorganisms instantaneously. A one-per-cent. solution of hydrochlorate of quinine, added to the blood in the proportion of one part to four, permits of a continuance of the movements for one hour, the addition of the same quantity of a two-per-cent. solution kills the spirochætæ immediately. Strychnine (8:100,000) kills the spirochætæ. Carbolic acid in one-per-mille solution also kills the microorganisms. Solutions of 1:3,000 of the protochloride or the nitrate of mercury immobilize the spirochætæ instantaneously, and 1:4,000 solutions of the same substances produce a like effect after a short interval. According to Seyliger, a sublimate solution, even as weak as 1:30,000, produces a noticeable effect. Alcohol of 12°, added in the proportion of one part to eight parts of blood, arrests the movements in a few hours, but the same quantity of 20° alcohol produces this result almost immediately. When exposed to the vapor of alcohol of 60°, or to that of chloroform, the movements of the spirochætæ in the blood are arrested in the course of half an hour. Benzoic acid in 1:5,000 strength produces no effect. Naphthol-β in 1:6,000 solution produces a marked effect upon the mobility of the microorganisms, but unfortunately this substance is soluble with great difficulty. Fowler's solution, 1:2,500, is without any apparent effect upon the spirochætæ. Pyoktanin does not begin to act upon the microorganisms until it is in the proportion of 1:1,500, and the same is true of gentian violet. Fuchsin acts even more feebly. Methylene blue arrests the movements of the spirochætæ very rapidly when added in the proportion of only 1:10,000 and at the same time it imparts to them quite an intense stain. The passage of an electric current, even a very weak one, arrests the movements quite speedily.

While some substances act upon the spirochætæ only in killing them, that is to say, in arresting their movements, others, such as glycerin, caustic potash, and distilled water, cause their complete disappearance.

The facts which we have just been considering demonstrate to us that on the one hand very feeble influences, such as condensation or dilution of the blood containing the spirochætæ, or the addition of blood, either different or homogeneous, produce very evident effects upon the movements of the microorganisms, while on the other hand these microbes differ greatly from others in their behavior to certain

agents; thus, they are strongly influenced by certain substances such as potassium iodide and glycerin, but are quite resistant to the action of others, such as hydrochloric and salicylic acids, quinine, etc.

The best fluids for the preservation of spirochætæ are strong solutions of sodium chloride, Müller's fluid, and especially osmic acid, which preserves not only the red blood cells and other protoplasmic elements, but also minute organisms as delicate as spirochætæ.

Up to the present time we have discovered no media suitable for the cultivation of Obermeier's spirochætæ, and the hopes in this regard which were inspired by Robert Koch have not been realized. According to the observations of Albrecht, only the blood of persons affected with relapsing fever presents a favorable soil for the growth of these microorganisms. This investigator took the blood of a patient with relapsing fever during the apyretic period, when no spirochætæ at all could be detected in it, and made preparations from it in the moist chamber. At the beginning no spirochætæ could be found on the most careful examination repeated on several successive days, but suddenly they were found in enormous quantities. Their appearance was always, however, several days (two or three) later than the occurrence of a new febrile paroxysm in the person from whom the blood was taken. The average duration of this period of latency of the spirochætæ was from five to six days. Albrecht, however, asserts that the germs of the spirochætæ circulate in the blood during the period of apyrexia. Similar results, as regards the development of the spirochætæ, to those obtained outside of the body have been obtained in blood taken from a patient in the apyretic period by Lachmann and Gerhardt. Gabritchevsky has also observed multiplication of spirochætæ in the blood. Up to the present we do not know positively in what manner and by what elements reproduction of the spirochætæ takes place, whether it occurs by means of segmentation or sporulation or in some other manner. Among the different modes of reproduction we may assume that segmentation is the least probable because of the sudden appearance of large numbers of the microorganisms in the blood in which up to that time they had not been found at all (Albrecht).

In order to obtain a more precise notion of the rôle of the spirochætæ in the production of relapsing fever, it will be interesting to recall certain inoculation experiments. Minkh and Motchoutkovsky were the first to demonstrate clearly the etiological rôle of the spirochætæ in relapsing fever. Minkh inoculated himself through a wound in the arm with the blood of a patient suffering from this fever, and obtained positive results. Motchoutkovsky inoculated others, having previously obtained their consent to the experiment,

with blood containing spirochætæ, with equally positive results. Similar experiments have since been repeated in their own persons by Metchnikoff and Doroshevsky, the results in each case being confirmatory of the etiological relationship between the disease and the microorganisms. Inoculation experiments made on the domestic animals which commonly served for this purpose (dogs, cats, pigs, rabbits, guinea-pigs, rats, mice, sheep) have usually been attended with negative results, but H. Vandyke Carter and Robert Koch have succeeded in exciting symptoms of relapsing fever in monkeys (Macacus radiatus, Lemnopithecus entellus) by giving them subcutaneous injections of defibrinated blood, containing spirochætæ, taken from a patient with relapsing fever. In the same way they also succeeded in transmitting the disease from one monkey to another. In Carter's experiments twenty-two out of thirty-one monkeys submitted to experiment contracted relapsing fever. The intensity of the disease in the men from whom the blood was taken had no apparent influence upon the results of the inoculations, but the passage of the infectious principle through the organism of the monkey seemingly increased its effect very materially. The period of incubation varied from thirty to one hundred and twenty-six hours, the mean being ninety hours. The fever attained its maximum intensity, during the first day of the disease, within a period of from three to twelve hours. The duration of the fever was usually quite short (from six to eighty-six hours). Some hours after the fall of temperature and after the spirochætæ had disappeared from the blood, the temperature rose again for a period of from six to twelve hours. Sometimes, in the more severe cases, this elevation of temperature was observed only after three days and a half, but these were not true relapses such as are observed in man. One attack of relapsing fever did not confer immunity in the case of animals, for an injection of blood from a patient with relapsing fever made into the subcutaneous tissues of a monkey which had just emerged from an attack or had had one some time previously, never failed to excite a new febrile paroxysm. The spirochætæ developing in the blood of monkeys differed in no respect, neither in their form nor in their movements, from those found in the human subject. Carter, however, thought that they were slightly shorter and had fewer spirals. Their increase in number during the height of the fever and their disappearance in the apyretic period corresponded in every respect to the same phenomena observed in man. Autopsies in these cases revealed the presence of spirochætæ in the brain, the lungs, the liver, the spleen, the kidneys, and the skin.

Following Carter and Koch, inoculation experiments in monkeys were repeated with the same results by Metchnikoff, Soudakevitch,

Tiktin, Gabritchevsky, and Ivanoff. These last-named studied especially the question of immunization in animals, and we shall return to the consideration of their experiments at the proper time and place. Tiktin examined bedbugs which had filled themselves with the blood of men and monkeys suffering from relapsing fever, and found that the blood of these insects contained spirochætæ for a period varying from eighteen to seventy-seven hours after they had gorged themselves; the spirochætæ were sometimes free, sometimes enclosed in cells; sometimes they were completely immobile, and sometimes they preserved their movements for three-quarters of an hour. The blood taken from eight bedbugs which had fed upon an infected monkey was injected into another monkey. Sixty-four hours later spirochætæ were found in the blood of this second animal. The monkey became ill, the malady lasting about six hours. During the precritical elevation of temperature (to 40° C.) no spirochætæ were to be detected in the blood. After this fever the apyretic period set in with a temperature of 36.3° C. It is very plain that we are here met with the question, how far it is possible to identify affections of this kind with true relapsing fever in man, although they are certainly provoked directly by inoculations of blood taken from a patient with this disease. However this may be, the experiments just referred to indicate to a certain degree the possibility of the transmission of the disease through the intermediary of parasites so widely diffused as are bedbugs. Certainly the human organism and that of animals, even those so nearly related to man as the monkey, cannot be regarded as identical, and for this reason we cannot be expected to find an entirely similar evolution of the same malady in the two organisms, even when the exciting cause is the same. Nevertheless, in the cases under consideration the two affections are very similar in their essential symptoms (incubation, depression, fever, presence of spirochætæ in the blood, and even in certain cases relapse), and this speaks strongly in favor of a close relationship of the two.

The experiments in the way of infection of man by means of blood taken from subjects of relapsing fever and containing spirochætæ are even more convincing in this regard. Undoubtedly Motchoutkovsky succeeded in causing infection not only by means of blood containing visible and well-developed spirochætæ, but also by means of blood in which none were discoverable but in which one could assume the presence of their germs (which unfortunately we are not yet able to distinguish), and by means of blood in which the spirochætæ had been rendered immobile by the addition of quinine (one-tenth per cent.) or of alcohol. But the results of these experiments were in no way contradictory of the facts which we have just mentioned, and they are

furthermore very easy of explanation by supposing that the essential element of infection is represented by the spirochætæ, seeing that we know very well the difference in this respect between the various organisms and their germs or spores.

As regards the methods of obtaining the spirochætæ and preserving them in blood outside of the organism, we have yet to mention that employed for the first time by Pasternatsky and later by Karlinsky and others. According to this method blood containing spirochætæ is taken from patients suffering from relapsing fever by means of leeches, from which it is easy to express it later. In this way it is possible to preserve the spirochætæ in leeches for a longer or shorter period as may be desired. Unfortunately, however, this method, from which much was expected, has up to the present time given very moderate results as regards the study of the nature and properties of the spirochætæ and their germs.

In speaking of the relation between the presence of spirochætæ in the blood during the paroxysm and their absence at the apyretic period, and also of the reaction of these microorganisms in the presence of various influences, it will be proper to refer to the various causes which investigators have alleged in explanation of the disappearance of the spirochætæ from the blood during the crisis. This question is evidently one of very great and essential importance in view of the fact that its solution would show us what we have to do and towards what we must direct our efforts if we would treat this affection with success or be able to cut it short. The action of high febrile temperatures has been alleged by Heidenreich as the probable explanation of the disappearance of the parasite from the blood. The results of his experiments, indeed, and of those of others speak in part in favor of an influence of this kind. Nevertheless we cannot admit the exclusive influence of high temperatures and their immediate action upon the spirochætæ. A high temperature appears rather to be a coexisting agent and one auxiliary to other influences which have been designated by various writers as acting in the same direction and as possessing a great importance in this respect. It would certainly be difficult to deny any such action in the case of some of these influences at least. Motchoutkovsky has alleged the condensation of the blood which occurs during the crisis in consequence, according to him, of the sweating and the diarrhœa, and which exerts a very prejudicial effect upon the spirochætæ. The investigations of Traugott have, however, shown that the density of the blood diminishes gradually during the febrile paroxysm, especially after the crisis, and that there is merely a very slight and temporary increase in density during the sweating. Albrecht has noted that

there occur in the blood at a given moment of the existence of the spirochætæ an accumulation of the products of their activity which are injurious to themselves. Metchnikoff, who has contributed so much to our knowledge of the doctrine of phagocytosis, has argued in support of the theory that the spirochætæ are devoured by the cellular elements of the spleen, but we must confess that this theory does not very satisfactorily explain the cyclic evolution of the phenomena of this disease. Furthermore, the results of the experiments of others do not bear out Metchnikoff's assertions in all respects. This investigator founded his opinion in part on his personal observations, having seen the spirochætæ devoured by the cellular elements of the spleen, while those of other organs (liver, kidneys, bone-marrow) did not destroy the microorganisms; and in part on the experiments of Soudakevitch, who found that inoculated monkeys which had previously been subjected to a splenectomy died after an enormous multiplication of spirochætæ, while those in which the spleen was still present bore the disease much better. Tiktin, it should be mentioned, was unable to confirm the results obtained by Soudakevitch. In his experiments on the monkeys infected with the microbe of relapsing fever, those animals which had previously been subjected to splenectomy supported the infection in the same manner as those whose spleens were intact, and they recovered with equal promptitude. The animals of the second category, which had been infected and had acquired an immunity, retained this immunity after having had the spleen removed as long as did others with spleen intact.

Recently the question has been raised of bactericidal substances elaborated by the organism during infections of various kinds and which are alleged to destroy the generators of the infection. The experiments of Gabritchevsky have shown that at determinate periods in the course of relapsing fever there do actually appear in the blood certain substances possessing very pronounced bactericidal properties in respect to spirochætæ. If to the blood serum of a patient in the febrile stage of relapsing fever we add some serum from the blood of another patient who has passed through an attack of the disease, we see within one-half to one hour at a temperature of 37° C. (98.6° F.) and within from two to four hours at the ordinary temperature of the room, that all the spirochætæ become immobile and deformed, and finally perish utterly. It is very remarkable, however, that high temperatures favor most of the influences which we have just mentioned. Thus the increase in the injurious products of activity of the organisms, even leaving aside those elaborated by the human economy, as well also as the increase in phagocytic action and the production of bactericidal substances, takes place much more intensely at high tem-

peratures than at the normal temperature of the body. A more exact and detailed analysis of all the agents above mentioned would without doubt be very useful, in view of the importance of the question; but unfortunately this is a very complicated subject, the study of which has only just begun, and which presents still many vague and contradictory points.

In speaking of the relation of spirochætæ to relapsing fever we think it will be interesting to note that Steel has observed in horses in India a disease which bears a striking resemblance to relapsing fever in man, and which is almost always followed by a fatal result. Horses and asses alone are naturally subject to this disease, but it may be transmitted by inoculation to monkeys and dogs and runs in them the same course as in horses, that is to say, the infected animals die. Steel found in the blood of animals suffering from this disease certain mobile spirilla resembling closely Obermeier's spirochætæ, which sometimes appeared in the blood in enormous quantities, disappearing to reappear in a new paroxysm. Sakharoff has also observed in birds an epidemic disease with typical course and elevated temperature depending upon the presence in the blood of microorganisms resembling greatly Obermeier's spirochætæ. In the living blood of these sick birds they twist about, turning round their longitudinal axis, sometimes with extreme rapidity, and disappear from the field of the microscope with the same rapidity as the spirochætæ of relapsing fever. In the spring of 1891 this disease terminated very rapidly by death, while in the autumn of the same year the birds survived the first stage and suffered later from an articular affection recalling acute articular rheumatism in man. At autopsy there were found an increase in volume of the spleen with softening of its parenchyma and certain yellow caseous nodules in the liver. No spirochætæ were found in the tissues or in the blood of these dead birds.

Other Etiological Conditions.

After this bacteriological review we will study the other conditions upon which the development and spread of the disease depend.

Relapsing fever, as has already been indicated, is a contagious and usually epidemic disease. The beginning of an epidemic is generally attributable to importation, sometimes very evident and sometimes so indefinite that the most careful investigation fails to demonstrate clearly the origin of the first case of the disease. The contagious element is incapable of long preservation or of renewal in all places where the germs have been imported outside of the human organism. As a general rule relapsing fever disappears at the

end of a longer or shorter period from the town or country into which it has been imported and does not again break out until after a new importation. It is only in Ireland and in certain parts of Russia, as well as in Egypt and India, that the disease appears to find a permanent home and to assume the character of an endemic, making from time to time excursions into other countries. But we must not forget that there may be pseudo-endemics, that is to say, false or artificial endemics resulting from a constant or very frequent reimportation from without. Thus the disease was observed for several years in London, and also in St. Petersburg and other cities where it has finally assumed the character of a true endemic.

The contagiousness of relapsing fever is quite marked, although it is far from being always of the same degree. Several epidemics of relapsing fever have been remarkable because of the enormous number of persons affected. Thus in Dublin alone 40,000 persons suffered from the disease in 1847–48. In the Russian army of the Danube, during the war of 1877–78 there were reported no less than 39,337 cases of relapsing fever. Other epidemics have been much more limited, there being not more than 1,000 or 500, or in some 30 or even 20 cases. Frequently, after epidemics have prevailed for one or two years, they disappear completely, as though they no longer found the conditions favorable for their existence among the inhabitants of the place.

Up to the present time we do not know exactly what constitutes, properly speaking, the chief cause determining the appearance of the disease. It has been attributed to telluric conditions, to contaminated drinking-water, to the crowding together of large numbers, and to the want of cleanliness which so often prevails in the habitations of the poorest classes. Night refuges, poorly ventilated, in which large numbers of wretched and filthy persons are congregated, serve preferably as foci in which the disease develops and whence it is propagated to other parts, and this, whatever may be the nature of the soil of the place in which the refuge is located or the character of the water which those harbored there drink. According to many authorities, the chief agent in the development and propagation of relapsing fever is to be found in the impurities coming from human beings and accumulating in large quantity. The remarkable fact has often been observed that relapsing fever and typhus fever exist side by side, the former affecting preferably the poorer classes and the latter those in more easy circumstances. Many English and Irish physicians (Steel, Murchison, and others) and also Germans (Griesinger, Bock, and Wyss) have attributed epidemics of relapsing fever to famine. They believe that relapsing fever is the true famine

fever, and they base this belief upon the fact that the great epidemics in Ireland, as well as those in Silesia, have always been preceded by years of scarcity. Famine constitutes without doubt a factor which contributes to the depression and weakening of the organism, which, in consequence, presents but little power of resistance to epidemic disease. This view, however, is not in accordance with the fact that many epidemics have occurred without relation to famine or scarcity of food. Furthermore, most of those affected with relapsing fever are, as Lebert has justly remarked, in no sense poorly nourished or cachectic. Several authors have asserted that a vegetable diet predisposes to infection by relapsing fever, but this is far from having been satisfactorily proven. Zorn, who carefully studied and well described the epidemic of relapsing fever in St. Petersburg in 1863–64, remarked that during Lent the number of patients was relatively smaller than before or after this period of abstinence.

When relapsing fever has once broken out in any place, it extends rapidly by means of contagion. The infection is observed the more frequently and is the more intense the more frequent and more immediate is the contact of the sick with the well. It is propagated then from epidemic centres in the formation of which bad hygienic conditions, such as the herding together of a large number of persons in dark and dirty dwellings, play an important rôle. In small apartments we often see all the members of a family affected in turn by the disease. The intervals which separate, under these conditions, the successive appearance of the disease in the different members of the family are, according to Lebert, very variable. In more than 27 per cent. of the cases this interval (*period of incubation*) is one day, in 16 per cent. two days, in 11 per cent. three days, in 5 per cent. four days, in 6 per cent. five days, in 6 per cent. six days, and in 4 per cent. seven days. Thus in 75 per cent. of all cases the disease manifests itself in the course of a week, and in 54 per cent. during the first three days.

The extension of epidemics in isolated houses and dwellings is much more marked in the case of relapsing fever than in that of other infectious diseases. Out of 46 homes invaded by this affection Lebert observed a total of 2 cases in 26 families and one of 3 to 6 cases in 20 families. In 16 of these 46 families two or three members fell ill on the same day; in the other families the different members were attacked at intervals of several days or weeks. It has been noticed that the women usually fall sick first, then the children, and only later the men become affected.

As personal relations, that is to say contact of the sick with the well, afford the most favorable conditions for the propagation of the

disease, it is easy to understand why physicians so often suffer, as also hospital attendants and nurses. The disease may be transmitted by the cadavers of persons dead of relapsing fever to those who have to do with the bodies, such as pathological anatomists and embalmers. Perls, a well-known German pathological anatomist, suffered from relapsing fever, which, according to Edinger, he contracted at an autopsy. This fact is in concord with the observations of Heidenreich, who found mobile spirochætæ in the blood of the cadaver of a man six hours after death from relapsing fever. Contagion may also be carried in clothing which has been worn by a patient and may thus be spread through the medium of laundries; this would explain the prevalence of the disease among washerwomen which has several times been noted (Cormac, 1842).

The occupation of apartments in which patients with relapsing fever have been may also contribute to the spread of the disease. I have had occasion personally to observe a very instructive instance of this sort during the Turco-Russian campaign of 1877–78. The officers of one company in a regiment of which I was surgeon-major, upon occupying a village which had been held by the Turks, put up at a house which seemed from external appearance to be better and more commodious than the others, but which was afterwards found to have been used by the Turks as a lazaretto. As soon as the officers had installed themselves in this house, the interior of which we may remark in passing was rather dirty, relapsing fever broke out among them; every officer, including the surgeon, was attacked, and one died. At the same time the morbidity in the other companies was slight and the character of the disease was very mild.

The disease usually passes from one country to another or from one district or city to another along the ordinary routes of travel, the rapidity of its progress being proportional to the frequency of communication between the two places. The epidemic of 1843 in Scotland invaded first the cities which were in closest relations with those in Ireland whence the disease had spread, and the epidemic of 1847 was at first confined exclusively to the Irish living in the Scotch cities. The first patients in London in the epidemic of 1847 were also Irish, and it was always by the Irish that the disease was imported into America, as we have seen above. From Siberia relapsing fever was imported into New Archangel, on the island of Sitka, in the ship *Tsesarevitch*, arriving October 2d, 1857, which brought six patients with the disease. These patients were taken to the hospital, and the new cases of relapsing fever were first among the nurses and servants employed in the hospital, passing later beyond the walls of this institution and invading the garrison.

It is not yet definitely established by what vehicle the contagious principle is conveyed from tho sick to the well, whether in the exfoliated epithelium, in the sweat or other cutaneous secretions, the hair, the saliva, the nasal mucus, the urine, or the fæces; nor do we know through what channel it enters the body of the healthy, whether by the skin, the respiratory passages, or the digestive tract. One thing we have definitely learned within a comparatively recent time, namely, that the contagious principle exists in the blood, and that it can be transmitted from the sick to the well in the latter provided this fluid be taken from the patient during the febrile paroxysm. On account of this fact it has been believed that the ordinary parasites of man play a more or less important rôle in the spread of the contagion of relapsing fever.

As to the other conditions bearing upon the etiology of the disease, we must content ourselves with the few remarks which follow.

Metereological Conditions.—The level of the ground water, climate, seasons, and weather exert no marked or definite influence in the development of relapsing fever. According to Hirsch, of the thirty-five epidemics occurring in Great Britain, Germany, and Russia, the disease prevailed most extensively in summer in twelve, and in winter in twelve, that is to say, the affection attained its maximum development in an equal number of instances under exactly opposite meteorological conditions. Epidemics have also occurred with as great frequency during hot and humid seasons as when the air was dry and cool. Some authors, however (Lachmann, Schmidt, and others), and especially Russian writers (Hermann, Reitlinger, Golinetz, Skvortsoff, and Likhatcheff) say that the greater number of epidemics occur during the winter. They explain this by the confinement and crowding together of the poor in their dwellings and in night refuges during the winter season.

As regards *sex* it has been generally noted that men are more commonly attacked than women, furnishing eighty per cent. of all the cases. This is readily explained by the fact that among the working classes the men are more often obliged to mingle with others, gaining their living outside of their homes.

As regards *age* those between fifteen and thirty years furnish the greatest number of cases, partly because this age is the one in which men are more often exposed to certain injurious influences, as in wandering about in search of work, and partly because relapsing fever follows in this respect the general rule of affections of this nature. No age, however, even the most advanced (we have seen a fatal case of relapsing fever in a woman seventy-eight years old) or the youngest (cases have been observed in intrauterine life), is com-

pletely immune to this affection. Of the two extremes of life, however, children are more apt to suffer than adults past the age of fifty. The age at which women more commonly suffer is as a rule somewhat higher than in the case of men, a fact which we have also observed in respect of typhoid and typhus fevers. It is difficult to account for this, but it may possibly be due to the fact that women of somewhat advanced age more nearly approach men in the conditions of their existence, being more exposed at that time to the specific injurious influences.

Trades and *professions*, except those above indicated (laundresses, etc.), do not exercise any special influence.

The disease has often been observed in *pregnant women*, in whom it commonly determines abortion or premature labor, the child being born dead or dying soon after birth. Albrecht often found the fœtus suffering from relapsing fever, having spirochætæ in its blood. In the mothers the disease quite commonly runs a benign course.

In its *relations to other diseases* relapsing fever acts as an autonomous disease, having no special connection with any of them. It does not exclude the possibility of the coexistence of any other disease, either during its course or after its subsidence, nor does the previous existence of any other disease insure immunity against an attack of relapsing fever. Lebert believed that the tuberculous rarely contract relapsing fever, but this view lacks support. It has been noticed that relapsing fever often coexists with certain other diseases, especially malarial fever, which sometimes precedes, at other times follows the relapsing fever. The latter disease, however, is frequently imported into regions where there are no special conditions favorable to the development of malaria, or where this affection is entirely unknown. Cerebral meningitis and dysentery have often been observed to exist coincidently with relapsing fever, but more frequently the latter occurs with typhus and typhoid fevers, especially typhus, which has very often been observed to precede or more rarely to follow an epidemic of relapsing fever. This coincidence suggests that the two diseases have much in common as regards the conditions favorable to their development. It is indeed very remarkable that a person who has passed through an attack of one of these diseases has often to suffer from the other, typhus fever more commonly following than preceding relapsing fever. According to Lebert's observations successive attacks of these two diseases are more often observed in patients between fifteen and forty years of age, less frequently before puberty, and in about one-fifth of the cases between the ages of forty and sixty years. The interval between the attacks of relapsing and typhus fevers varies from a few weeks to several months. It is note-

worthy that in these cases the mortality of typhus fever is only about one-half as great as it is when the disease occurs unassociated with relapsing fever. Cases have been observed of the coexistence of relapsing and typhus fevers in the same person, and also of relapsing and typhoid fevers (Botkin-Borodoulin). It has also been remarked that the mortality in these cases of coexistence of the two diseases is not increased, but on the contrary the death rate is below that of either disease when occurring alone.

Those who have once suffered from an attack of relapsing fever are not thereby rendered immune to subsequent attacks, or at least the immunity conferred by one attack is of very short duration. Christison suffered from three attacks in the course of fifteen months, and Perls also had a second attack which followed the first within less than a year. Litten has seen five cases of reinfection occurring within a period of from twenty-nine days to four months after the first attack. In this connection a case observed by Motchoutkovsky is interesting: A young girl suffered from a first attack consisting of four paroxysms; after an interval of twenty-three days she again fell ill and had three distinct febrile paroxysms; after this there was an interval of seventeen days when she fell ill for the third time and passed through two paroxysms. According to Motchoutkovsky two weeks marks the limit of the immunity conferred by one attack of the disease. In inoculation experiments on monkeys, Carter and others were able to induce a second infection. These facts are of considerable importance, since they indicate the necessity of isolating relapsing-fever convalescents from those passing through an attack in order to prevent a second infection.

Symptomatology.

The latent period of infection, called the *period of incubation*, lasts from five to eight days according to most writers, among them Motchoutkovsky, Spitz, Schmidt, and others. But these limits are not absolute, and the period may be either longer or shorter. Perls wounded himself in performing an autopsy on the body of a person who had died of relapsing fever, and the attack began in him at the end of seven days. Minkh accidentally inoculated himself on the forearm near the wrist from a pipette containing spirochætæ, and he suffered from an attack of relapsing fever which began six days later. In animals, as we have seen above, the period of incubation is in general shorter than it is in man.

Prodromes are wanting in most cases, and when they do exist they consist simply of the ordinary phenomena observed during the period

of invasion of the typhoidal diseases, such as general malaise, lassitudé, anorexia, headache and weight in the head, insomnia, etc. These symptoms last but a short time, a few hours, or rarely two or three days. That which especially characterizes this disease is its rapid, often almost sudden invasion, and this even in cases in which prodromes have existed.

The attack begins ordinarily in the morning or during the day, rarely in the evening or during the night, by an intense fever (39° to 40° C.—102.2° to 104° F.) often accompanied by a violent chill, lasting perhaps an hour or longer. In certain cases this chill may be repeated. In other cases there is only a succession of more or less marked chilly sensations. The patient is forced to take to his bed on account of the extreme weakness, soon accompanied with headache, either frontal or temporal, and often with vertigo, nausea, and vomiting, and with violent pains in the back and all the members (especially in the lumbar region and in the lower extremities). The patient suffers greatly from thirst and from a hyperæsthesia of sight and hearing. Insomnia is usually very troublesome and there is great restlessness at night.

In a few days the headache assumes a throbbing character. The skin becomes hotter and sometimes a little moist. The agitation increases. The temperature rises to 40° C. (104° F.) and higher, especially in the evening, sometimes reaching 41° or 42° C. (105.8° or 107.6° F.) at that time, but with quite marked morning remissions.* From the beginning of the disease the pulse is very frequent, being 100 or even more from the onset, and soon rising to from 120 to 140 or more in the minute.

The patients complain of a bad taste in the mouth, and their breath is fetid. The tongue, at first moist and covered with a thick white coat, later becomes dry. Constipation is present or sometimes a slight diarrhœa. The patients often suffer from prolonged vomiting and from the second day frequently complain of a feeling of weight and other disagreeable sensations in the epigastrium and in both hypochondriac regions. Soon actual pain, of greater or less intensity, spreads over the entire left hypochondrium. The liver and the spleen increase notably in volume and become painful on pressure. The progressive increase in size of the spleen especially may often be followed from day to day, or almost from hour to

* As a rule the temperature in relapsing fever rises to a higher level than it does in other typhoidal diseases. The figures which I have collected from the Warsaw clinic give the following averages: For relapsing fever, 40.75° C. (105.35° F.); for typhus fever, 40.36° C. (104.65° F.); for typhoid fever, 40.37° C. (104.66° F.).

hour, by means of percussion and palpation, and the organ quickly passes the border of the false ribs.

Myalgia is very marked. The patients complain of pain in the muscles even during repose, but this becomes much more pronounced during movement or when pressure is made on the soft parts. This is more pronounced in the muscles of the occiput, of the back, of the chest, of the abdomen, of the upper and lower extremities, and especially in the calves of the legs. The pain is cutting, lancinating, piercing, or without any special character. On account of the pain the patients keep themselves almost motionless, but there is not that apathetic facies observed in typhus and typhoid fevers. Delirium is rare, and notwithstanding an extreme weakness the patients retain consciousness.

Examination of the skin reveals ordinarily no eruption. Occasionally the presence of petechiæ has been noted, especially over the hypogastrium, and sometimes we see facial herpes and, in the later paroxysms, sudamina. It is not uncommon in the ordinary cases to see an icteric coloration of the skin by the third or fourth day. The fæces, however, remained colored. The urine is febrile in appearance, and sometimes contains albumin and casts.

The prostration, restlessness, fever, and thirst are at their maximum on from the fourth to the sixth day. A very marked sensation of tension in the epigastrium causes oppression and dyspnœa. From the beginning of the attack we find the spirochætæ in the blood (see page 455).

Crisis.—In the midst of these grave symptoms, when the disease is at its height (five, six, or seven days after the onset), suddenly all the morbid phenomena grow less. A profuse sweat comes on and the temperature falls 4° to 6° C. (7° to 11° F.) in the course of a few hours (from two to twenty-four), most commonly in the period from evening to morning. The frequency of the pulse diminishes, falling sometimes below the normal. The headache becomes less severe, and the respiration becomes freer. The pains disappear or diminish greatly as a rule, but in some cases they persist with sufficient intensity to cause the patient much discomfort. Sleep becomes quieter, the appetite returns, and the excessive thirst disappears. The stools become normal and the volume of the liver and spleen is reduced. Soon the patient's strength returns to such a degree that he leaves the bed, and some even quit the hospital at this time despite the warning of the physician that a relapse is liable to come. During the crisis, or the hours preceding it, the spirochætæ usually disappear from the blood.

Sometimes, though rarely, the morbid phenomena do not disap-

pear so suddenly and rapidly, but more deliberately. The patient still experiences considerable lassitude, a slight elevation of temperature persists, there is a painful sensation remaining in the extremities, etc. But these symptoms all disappear finally.

The apyrexia ordinarily lasts only a few days, in many cases seven days, sometimes more rarely only four or five days, and rarely fourteen days. In certain quite rare instances the apyrexia begins a definitive convalescence, that is to say, the disease limits itself to a single paroxysm.

The *second paroxysm*, or the *first relapse*, comes on as suddenly as did the first, most commonly during the night, though occasionally in the morning or afternoon. The patient is seized again with a violent chill or a succession of chilly sensations, although it must be mentioned that occasionally these initial symptoms of the relapse are entirely wanting. The violent pain in the extremities and in the head, the malaise, the vomiting, the high fever and greatly accelerated pulse, the increase in size of the liver and spleen, all these symptoms of the first paroxysm are faithfully retraced. The spirochætæ reappear in the blood, to disappear again, as in the first attack, at or during the approach of the crisis. The duration of the second paroxym is usually shorter than that of the first, being from three to five days, sometimes only two or three. During the paroxysm we observe marked morning remissions and evening exacerbations. The terminal crisis is often preceded by a so-called precritical period, or false crisis, after which the temperature rises again for a brief period. In other cases we observe, from twelve to twenty-four hours before the crisis, a very marked aggravation of all the symptoms—the "perturbatio critica."

The crisis appears, as in the first attack, most frequently in the evening or night. We observe then an abundant sweating, and the morbid phenomena progressively diminish in intensity. The following day usually the temperature and pulse fall below normal, and the patient enters into definitive convalescence; or else, after the expiration of a certain time (generally from four to seven days, rarely more), the third attack appears with the same features as those of the preceding paroxysms above described. The intensity of the symptoms in this attack is usually less, and the duration of the paroxysm is shorter. In certain epidemics a third attack is common, in others it is rare. In most cases, when it occurs, it is followed by recovery, but sometimes (Motchoutkovsky, Litten, and others) there are still other relapses.

Convalescence.—The time of complete restoration to health after relapsing fever varies in different cases according to the number and

the intensity of the relapses. If the course of the disease has been favorable the patient is able to resume his ordinary occupations in about two weeks after the subsidence of the last paroxysm, or in from four to eight weeks after the onset of the fever. In other cases convalescence is more prolonged. The emaciation, general debility, anæmia, and various complications, of which we shall have to speak later, are the usual causes for the retardation of convalescence.

During the period of convalescence, as we often see in typhoid fever, the temperature may rise for a time (complementary fever) without the occurrence of any complication, this seeming to be a last feeble reaction of the organism against the infection. The pains in the muscles and bones may also reappear from time to time during convalescence. Finally we may observe in convalescence some desquamation of the skin, and sometimes also œdema of the cellular tissue and ascites.

Death may occur from general exhaustion and collapse, in cases in which the intensity of the pathological process is very great; it occurs more frequently in the course of or after the second paroxysm, but is most commonly caused by some complication, such as pneumonia (see below). In certain cases the patient dies in the course of the primary attack, as a result of the excessive temperature and consequent weakness of the heart. In such a case the sweating stage does not appear, all the symptoms increase in gravity, and the patient falls into a typhoid state, with prostration, stupor, deafness, delirium, a burning heat of the skin, dryness of the tongue, which is covered with a dark coat, and involuntary stools. In certain cases we see continual vomiting, in others it is the comatose or convulsive state which predominates. Finally, cases are met with in which, after a certain period of calm, a sudden general prostration, sometimes accompanied with vomiting, ensues and the patient dies suddenly.

Bilious Typhoid.—In the preceding description we have endeavored to present a picture of the most common form of relapsing fever, of that which is usually described under this name. But alongside of this ordinary form of relapsing fever we sometimes see others presenting more or less pronounced deviations from the type, due either to complications which may supervene or to a certain special degree of virulence of the infectious principle. Among these atypical forms of relapsing fever we have first to mention that in which jaundice occurs as a complication, a form which Griesinger has described under the name of "bilious typhoid." Although some doubt might at one time have been felt whether this was really a form of relapsing fever, there can now no longer be any question concerning the identity of the two affections. Recent researches have shown in general

a complete resemblance in the clinical picture as well as in the anatomical lesions between relapsing fever and bilious typhoid. Furthermore, the presence of Obermeier's spirochætæ has been noted in the blood of those suffering from bilious typhoid (Heidenreich, Motchoutkovsky, and others). And finally Motchoutkovsky has succeeded in producing the ordinary form of relapsing fever by inoculation with the blood of a person suffering from so-called bilious typhoid. It is interesting to note in passing that he did not succeed in reproducing the icteric form of relapsing fever but only the ordinary form. The addition of the symptoms of pernicious jaundice to those of relapsing fever impresses a seal of special gravity upon the latter, rendering its course much more dangerous and greatly increasing its mortality.

Jaundice of mild degree is not rare even in the ordinary form of relapsing fever, and sometimes it even becomes very intense in this form, this being the result not only of mechanical retention of bile by reason of the catarrh of the duodenum and bile ducts, but also of the action of the infection upon the hepatic tissues. The liver is, as we shall see, often profoundly affected and frequently presents changes which are peculiar to pernicious jaundice (acute yellow atrophy of the liver).

The other symptoms of relapsing fever are likewise more pronounced in the icteric form of the disease. The general condition may also be profoundly disturbed as manifested by stupor, delirium, convulsions, and hemorrhages from the skin and mucous membranes. In this form the patient sometimes dies during the primary paroxysm, the duration of which is often longer than in typical cases.

In addition to the icteric form of relapsing fever (bilious typhoid) we distinguish another form, called *syncopal,* with which are associated chiefly cardiac lesions, and an *abortive* or, more correctly, *incomplete form.* In the latter we find but a single mild and short paroxysm, or perhaps two, speedily followed by convalescence. Meschede, in his description of the epidemic of 1879–80 at Königsberg, says that of three hundred and sixty patients thirty-eight had very mild attacks. These complained only of a slight general malaise with rheumatic pains, and if there had not been an epidemic reigning at the time they would not have been recognized as cases of relapsing fever.

Special Symptoms.

Temperature.—The most characteristic symptom of relapsing fever is the course of the temperature, its rapid rise, the existence of hyperpyrexia for a certain number of days, and then its rapid fall to the

normal point or below. Then, after a fever-free period of longer or shorter duration, a new attack appears, the evolution of which resembles the first—and so on. All this occurs more or less regularly at the end of a certain definite number of days, and may be repeated several times. These repeated attacks (relapses) are so characteristic of this disease that they have given to it its name. A relapse occurs in ninety-nine per cent. of all cases. Usually there is but one relapse, that is to say, two febrile paroxysms; more rarely there are three, and very exceptionally four or five. Some authors have recorded six or even seven paroxysms of fever. We find in the first decennial report of the Botkin Barracks Hospital at St. Petersburg that two patients in the hospital during the epidemic of 1882–83 had each seven attacks; one of these patients was between fifteen and twenty years of age, the other between thirty-five and forty. During the epidemic of 1890–91 there were two patients who had each six attacks; one of these patients was sixteen years old, the other twenty. Recovery took place in each of these four cases. Mme. Pavlovsky reported in the *Meditsinskoïe Obozrenie*, No. 2, 1878, a case in which there were six febrile paroxysms between March 21st and May 25th. The interval of apyrexia was six days after the first attack, twelve after the second, seven after the third, eight after the fourth, and seven after the fifth. The longest paroxysm (six days) was the fourth, the shortest (two days) was the fifth, the latter with the highest temperature (41.4° C.—106.5° F.); the sixth paroxysm, with a temperature of 41° C. (105.8° F.), lasted three days.

The various epidemics differ markedly in this respect. In some the occurrence of two attacks only, that is to say, of only one relapse, was the almost invariable rule, while in other epidemics there were ordinarily several paroxysms. Thus at St. Petersburg, according to observations in the Botkin Barracks Hospital during the epidemics of the last ten years, the number of attacks in the cases ending in recovery was as follows: in 1882–83, 32.5 had only one attack, 35.5 had two, 25.5 had three, and 6.5 per cent. had more than three attacks. During the epidemic of 1885–86, 42.5 per cent. had one attack, 35.2 had two, 19 had three, and 3.2 per cent. had more than three attacks.

In 1890–91, 34.85 per cent. of the patients had one attack, 39.4 had two, 22.15 had three, and 3.41 per cent. had more than three attacks. Of the fatal cases treated in the hospital during the epidemic of 1890–91, there had been in 50.48 per cent. one attack, in 39.8 two, in 7.76 three, and in only 1.94 per cent. had there been four attacks. In the report of the temporary Municipal Hospital at St. Petersburg we find that during the epidemic of 1880–81, 65.7 per

cent. of those who recovered had had but one attack, 25.7 had had two, nearly 5 per cent. had had three attacks, and 2.6 per cent. had had four. The total number of those who recovered was 342.

The first attack of fever lasts ordinarily from five to seven days, rarely from three to four, or from eight to twelve days (chart No. 1). As a rule the duration of the first attack is longer and the condition of the patients during it is graver than in any of the following attacks, and of the latter each is usually shorter and milder than the one which precedes. The duration of the apyretic intervals is usually in inverse ratio to the duration of the febrile attacks. According to the observations of Motchoutkovsky the average duration of the febrile attacks is as follows: The first attack, 6.75 days; second, 5.5 days; third, 3.25 days; fourth, 2.12 days; fifth, 1.66 days. According to Meschede (1879–80), the first attack lasts on an average from 6 to 7

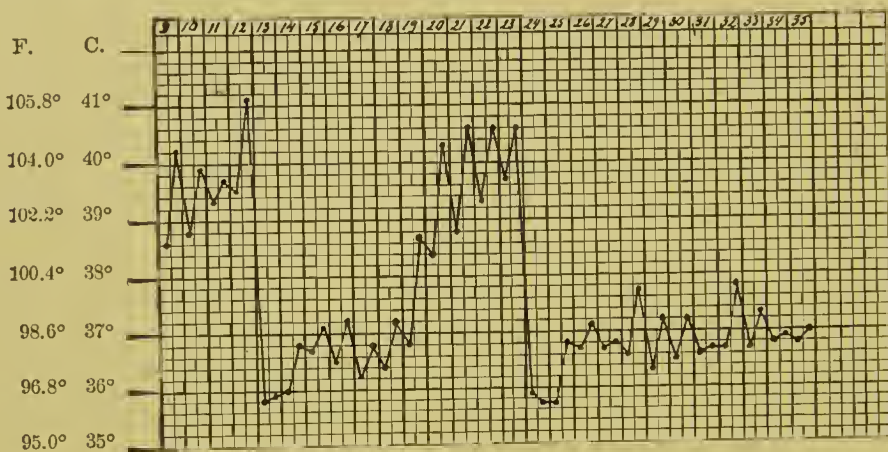

CHART No. 1.—Relapsing Fever. The figures in the upper line in this and the succeeding charts indicate the day of the disease.

days; the second from 4 to 5 days; the third from 3 to 4 days; the fourth from 1 to 2 days; and the fifth from a few hours to one day. Seyliger in his statistics of 200 cases studied during the epidemic of 1895–97 gives figures only for the second and third paroxysms, the first having seldom been observed during its entire course. In these cases the average duration of the second attack was 4.15 days; that of the third, 3.05; that of the fourth, 2.7.

According to Motchoutkovsky the average duration of the apyretic intervals is: the first interval, 5.25 days; the second, 6.16 days; the third, 9 days; and the fourth, 10.5 days. According to Meschede the figures are: for the first interval 7 to 8 days; for the second 9 to 10 days; and for the third 11 to 12 days. From Seyliger's statistics we find the average duration of the first apyretic interval 6.95 days; second, 8.45, and the third, 8.7 days.

Seyliger computed the average duration of each complete cycle of

the disease, that is to say, of the time necessary for the complete development of the infection by spirochætæ, and for its characteristic manifestations (the first period or cycle embracing the period of incubation and that of the primary febrile paroxysm; the second cycle embracing the first apyretic interval and the first relapse; the third the second apyretic interval and the second relapse, or third febrile paroxysm, etc.). From a study of the figures so obtained he formulated the following conclusions: 1. The duration of each of the corresponding cycles is an invariable quantity in a very large number of cases. 2. With each succeeding cycle the number of febrile days diminishes, while that of fever-free days increases. 3. The increase in the number of apyretic days is somewhat greater than the diminution in the number of febrile days, so that each new cycle is somewhat longer than the preceding; this increase of the apyretic interval takes place not wholly at the expense of the preceding paroxysm, but is due also in part to a retardation in the appearance of the succeeding paroxysm, the latter being probably due to the fact that the organism contains during the apyretic intervals certain substances which hinder the development and evolution of the spirochætæ from embryonal to adult forms. 4. The ratio between the duration of the first apyretic interval and that of the second febrile paroxysm is in 75.5 per cent. of all cases very nearly 2:1.7; that between the duration of the second apyretic interval and of the third febrile paroxysm in 81 per cent. of cases is more than 2:2.8; and that between the third apyretic interval and the fourth attack exceeds 3:3.2. According to this author these figures will often enable us to determine with great probability the special period in the course of the disease with which we have to deal.

The course of the temperature is very characteristic and is the type of that form of fever called recurrent. The temperature rises very rapidly, beginning with the rigor, and attains 39° C. (102.2° F.) or higher. Even during the first day it may rise to 40° C. (104° F.) or over. In general during the first days of the disease the evening temperature rises to 40°, 40.5°, or 41° C. (104° to 105.8° F.), and in some cases we may observe a temporary rise in the evening to 42° C. (107.6° F.) or even a little higher. There is nothing in this high temperature of special gravity as regards prognosis, such as we are wont to believe in respect of other infectious diseases. The morning temperature is ordinarily lower than the evening by some tenths of a degree or possibly even a degree and a half Centigrade, but rarely is a difference of 2° to 2.5° C. (3.6° to 4.5° F.) observed. Thus if we take the mean of temperature of the primary paroxysm for from five to seven days we find very high figures. The temperature curve is

sometimes a continuous one, but usually it preserves the remittent type, falling in the morning to rise again in the evening. These remissions and exacerbations, however, do not always occur in the morning and in the evening, and they are not always regular. Careful observations have shown that oscillations of the temperature occur also during other portions of the day, and these oscillations may not be limited to tenths of a degree, but may be of an entire degree Centigrade, or even more. Thus occasionally we find that the temperature is higher during the late forenoon or in the afternoon than it is in the evening (Lebert). In certain rare cases the remissions are quite insignificant and the tracing for twenty-four hours remains at a nearly constant level. The maximum temperature may be found on either the first, the intermediate, or the final days of the paroxysm.

In certain cases, during the attack and especially towards its end, the remissions are so marked that the temperature may descend to the normal or even below, thus simulating the crisis (pseudocrisis); but ordinarily the temperature rises again towards evening to the preceding height, and observation will show that the spirochætæ have not yet disappeared from the blood. It not uncommonly happens that the termination of the attack is immediately preceded by considerable increase in the temperature, sometimes even up to 43° C. (109.4° F.), accompanied by chills—*perturbatio critica.*

In no other disease is the critical fall in temperature so great and so rapid as in relapsing fever. Ordinarily this fall begins in the night, more rarely in the morning. It ceases in most cases at the end of from six to twelve hours, and sometimes it is completed even by the end of three hours; a longer duration is observed only in exceptional cases. The mean fall of temperature is from 3° to 5° C., sometimes 6° and in certain rare cases 7° or more (5.4° to 12.6° F.). Thus the temperature may fall from 42° C. (104° F.) to 36°, 35°, or even 34° C. (96.8° to 93.2°). Sometimes this fall in temperature is followed by collapse. In fatal cases the fall of temperature during the crisis is sometimes as great as 9° C. (16.2° F.), from 40.4° to 31.4° C. (104.7° to 88.5° F.). The subnormal temperature that is frequently observed at the end of the crisis usually soon returns to the normal, especially in the evening. It often reaches the normal by the second day and remains there for from five to seven days. At the end of the apyrexial period the temperature gradually rises towards evening. Sometimes, however, after the critical fall the temperature continues to descend gradually during the following days. In general the temperature varies somewhat during the apyrexial period. Motchoutkovsky, as we shall see below, endeavored to establish certain rules in regard to the prognosis of the relapses upon the variable course of

the temperature during the period of apyrexia. These irregularities, however, lack the constancy necessary for applicability to all cases with any degree of certainty. The second paroxysm, or the first relapse, begins (as a rule on from the tenth to the fourteenth day of the disease), like the primary attack, with a rapid rise of temperature to 39° or 40° C. (102.2° to 104° F.) or even more. Often, usually in the morning, the patient is seized with chills. Then the temperature continues to rise, acting exactly as it did in the primary paroxysm. The maximum intensity of the fever is sometimes observed to occur during the second paroxysm, or first relapse (see Chart No. 2), and in most cases on the last day or the day before the last of that attack. The second paroxysm is, as we have said, usually shorter than the first (see Charts No. 3 and 4), but sometimes (very rarely) it may be

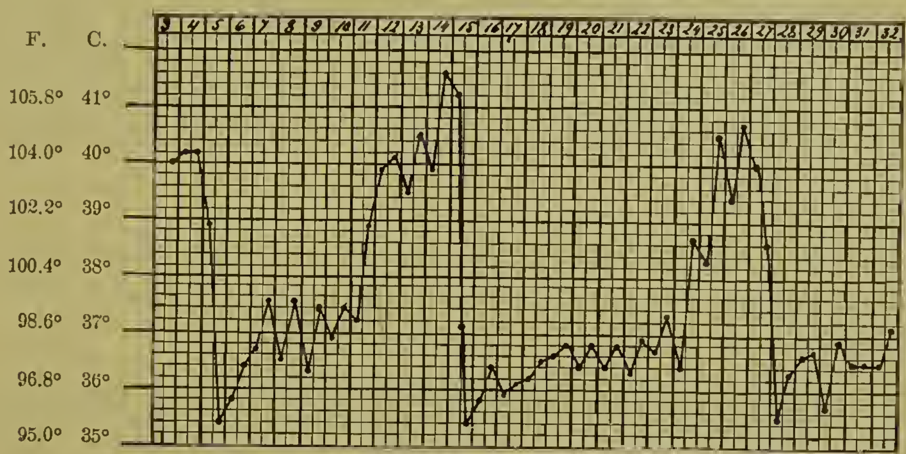

Chart No. 2.

longer than the first (Rosanoff, Loewenthal). The fall of temperature at the end of the second paroxysm has ordinarily the same critical characteristics, being as rapid and as extensive as that occurring in the first attack, and like that also it is followed by a profuse sweat. We may also meet with a pseudocrisis, false apyrexia, in the relapse as well as in the primary attack. According to Seyliger, these false crises are observed in the second paroxysm in 31.5 per cent. of the cases and in the third in 7.5 per cent. Ordinarily they are of short duration, from one-half to one day, and occur a short time before the true crisis.

As regards the third, fourth, and fifth paroxysms, the phenomena are usually the same as those just described, but of shorter duration. As we have said, the duration of each relapse is generally less than that of the preceding paroxysm.

A temporary rise of temperature, which may be very pronounced

but lasting only a day or less, may occasionally follow the true crisis. We also observe sometimes an elevation of temperature of short duration during the apyrexial period, but this is of no special importance unless it lasts longer than twenty-four hours. A rise of temperature of longer duration generally indicates the intercurrence of some complication.

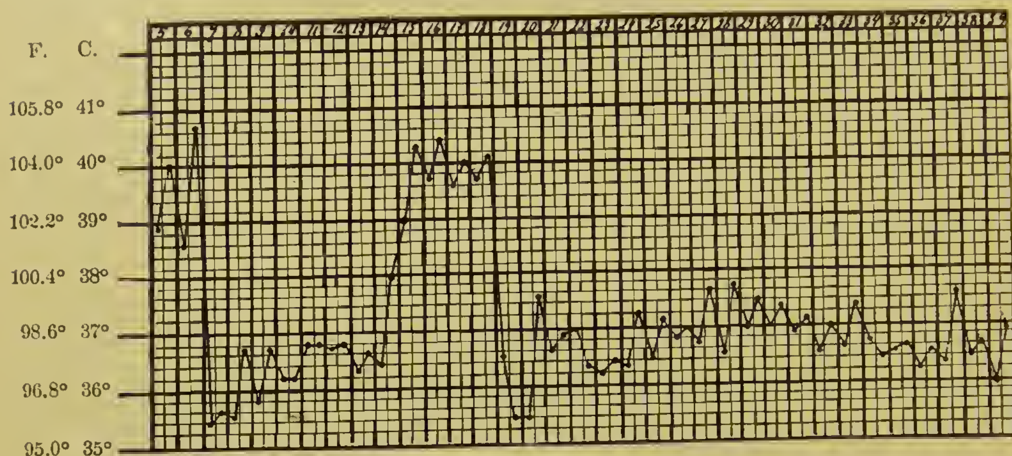

CHART No. 3.

In some cases, terminating in recovery, there is sometimes observed at the time that a possible relapse is due, a slight and temporary rise of temperature, lasting a day more or less, which may be

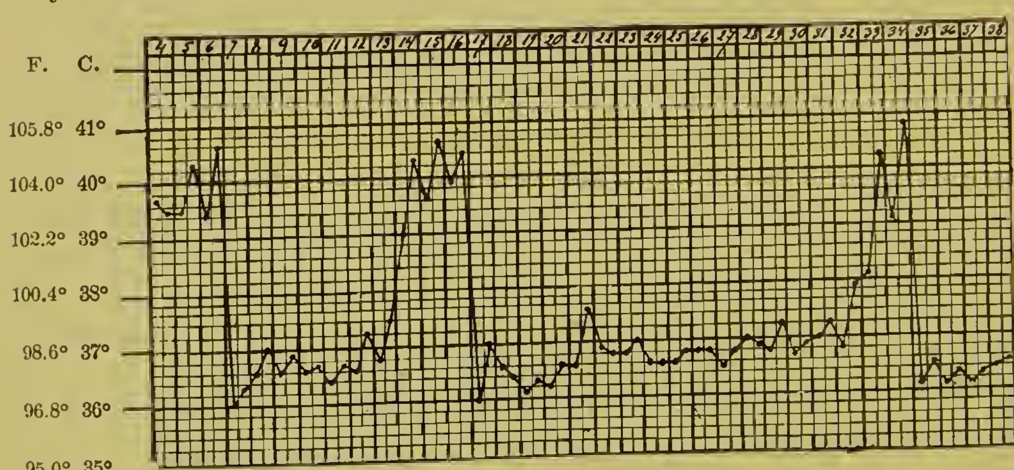

CHART No. 4.

regarded as an abortive relapse. In this connection we may remark again that in the very mild cases of relapsing fever the temperature of the first as well as of the second attack may rise much less rapidly and to a much lower level than in the ordinary cases (see Chart No. 5).

In respect of the period of apyrexia it is worthy of note that in certain cases, especially after the second and following attacks, the

duration of the period may be much longer than usual, even fifteen or sixteen days (see Chart No. 4).

The grave forms of relapsing fever which are complicated with icterus, have a very marked fever of relapse, with two, three, or even four (this is rare) cycles of each one paroxysm and one period of apyrexia. But in the gravest cases the course of the fever very often shows noticeable deviations in consequence of the numerous and serious complications which develop at the very beginning of the primary attack. For this reason also the first attack, in which the fever is very intense, may be considerably prolonged and be terminated by a crisis which is not at all frank. Even in these cases, however, we sometimes observe traces of a distinct remission with profuse sweating, soon followed by a fresh exacerbation. The temperature

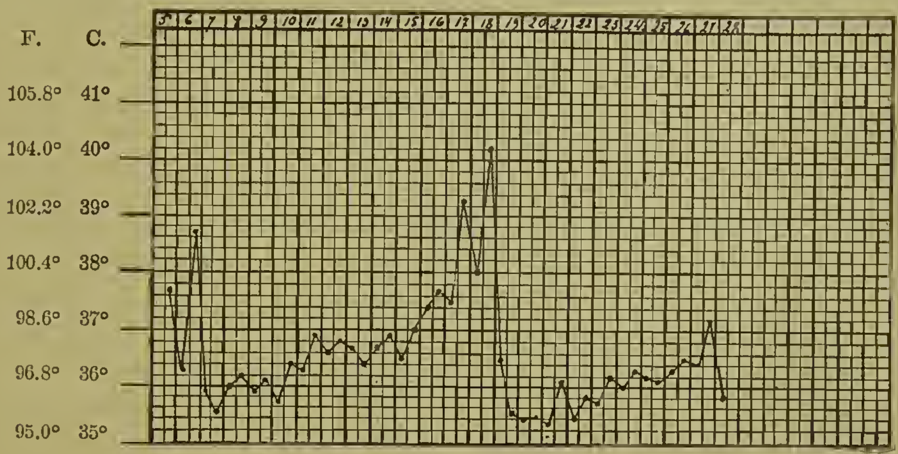

Chart No. 5.

may, as we have already seen, rise during a febrile paroxysm to a very considerable height, but sometimes the fever is not specially marked, oscillating for the most part between 39° and 40° C. (102.2° and 104° F.). Nevertheless, even in the cases of not excessive temperature, death may occur during the primary paroxysm with symptoms of prostration and collapse.

Pulse.—During the paroxysm the pulse rate runs parallel with the temperature and increases very rapidly in frequency, reaching, sometimes within the first twelve hours, the very considerable figures of 108, 116, or 120. In children the rate exceeds this by thirty or forty beats to the minute. At the height of the fever a pulse rate of from 120 to 140 is not rare, and it may occasionally reach even 160. The frequency of the pulse does not always correspond to the height of the temperature, but still there is always an acceleration of the pulse in the evening corresponding to the usual rise in the temperature at this time. Towards morning the pulse falls, together

with the temperature, from eight to twelve beats, or even more when the drop in temperature is very considerable. We sometimes see the maximum frequency of the pulse at the approach of the crisis, just as the highest temperature may also occur at this time.

Generally when the temperature is very high we find great excitation of the vascular system. The superficial arteries, such as the radial, the ulnar, and the carotid, may often present visible pulsations. In children we may sometimes even observe the head oscillating synchronously with the pulse.

The wave of the pulse at the beginning of the paroxysm is high, the arterial tension is considerable; but this soon diminishes, and the pulse becomes soft and compressible; the pulsations are short, sometimes trembling, and present the characteristics now of the pulsus celer or again of the dicrotic or even tricrotic pulse. At the height of the disease, when the general weakness of the patient is marked, the heart sounds become very feeble. The pulse then becomes filiform, irregular, and intermittent. Such a condition of the heart may result in sudden death (syncopal form).

Sometimes the vessels rupture, giving rise to more or less extensive hemorrhage. Epistaxis is frequent and may be so profuse as to demand plugging of the nostrils for its relief. Intestinal, renal, and muscular (rectus abdominis) hemorrhages are rare. We sometimes see ecchymoses and petechiæ in the skin, but these are seldom numerous. Metrorrhagia is rare, but when it occurs is one of the causes of abortion.

With the appearance of the critical phenomena the pulse soon falls to the normal rate. Sometimes it is still a little accelerated, but more frequently in the course of one or two days it descends even below the normal (to 50 or 40 in the minute). But sudden movements or excitement of any kind will cause it to rise quite rapidly to 100 or over. In rare cases (in the icteric form for example) the pulse does not rise much above the normal during the febrile paroxysm.

During the second paroxysm the pulse presents the same characters that it had in the first, and, just as in the primary attack, it does not always correspond to the course of the temperature.

Those who have passed through an attack of relapsing fever often suffer from a more or less pronounced anæmia, with pallor of the face, anæmic bruits in the vessels and in the heart, and sometimes, as a consequence of this anæmia, we find dropsy.

The *respiration* is ordinarily accelerated during the febrile paroxysm, not infrequently reaching 32 to the minute. The chief cause of this accelerated respiration is the infectious fever, for we usually see a return in frequency to the normal after the crisis. It must be re-

marked, however, that the elevation of temperature will not explain the increased frequency of respiration and even dyspnœa which may be observed in the course of relapsing fever. Although the critical fall in temperature generally diminishes the number of the respirations, the latter not infrequently, according to my observation, remain somewhat above the normal, at 24 to the minute perhaps. In many of these cases there is a bronchitis which may also have an influence in accelerating respiration. Another factor is doubtless the considerable elevation of the diaphragm due to the increase in size of the liver and spleen, and also the blood changes which take place in relapsing fever. Finally the weak state of the heart may in certain cases play a more or less important rôle. We shall discuss later the complications on the part of the respiratory passages.

Spleen, Liver, Stomach, and Intestine.—The spleen may be increased in size even from the stage of incubation (Friedreich). It enlarges with special rapidity by the second or third day of the primary attack. It becomes then two or three times its normal size, this increase being in all directions, the lower border sometimes passing below the border of the ribs by the width of a hand, so that the organ is very easily palpated. Ordinarily it is painful on palpation and percussion, but there may be pain in the left hypochondrium, independent of any enlargement of the spleen, which is increased by movements of the patient. During the crisis the spleen diminishes in size, often almost visibly, but it always remains slightly hypertrophied. In certain cases a very rapid decrease in size of the spleen has been noted during the occurrence of the profuse sweats. During the second attack the spleen behaves exactly as it did in the first, increasing during the fever and decreasing during the apyrexia. During convalescence it quite rapidly approaches its normal size, but it does not wholly return to its former dimensions until after the expiration of a considerable time. Several observers have noted a blowing murmur upon auscultation of the spleen at the height of the disease. The hyperæsthesia of the spleen frequently persists for quite a time, even into convalescence.

The liver also usually increases in volume during an attack of relapsing fever, and this increase may be quite considerable, but it is not so rapid as that of the spleen. The hypertrophied liver is also painful. During the period of apyrexia we may observe a slight decrease in size of the liver, but it remains somewhat enlarged for a considerable period.

Icterus occurs quite frequently but not always, and epidemics differ considerably in this respect. For example, in the epidemics of 1840–41 at Moscow and of 1843 in Scotland jaundice was very common and

was accompanied by grave symptoms (bilious typhoid). In other epidemics it was much less common. In ordinary cases there is but slight jaundice, but the most severe forms are almost always accompanied by icterus of great intensity. It appears either during the first attack, some three or four days after the beginning of the disease, and disappears during the crisis, or it occurs during the relapse and then increases the gravity of the disease. In mild forms the cause is the catarrhal state of the duodenum and the swelling of the mucous membrane of the common bile duct; in grave forms the parenchymatous affection of the liver is an important factor, as we find that the vomited matters almost always contain bile and also the stools are of a dark-brown color. But the mucous membranes, the skin, the tissues, and the urine are jaundiced. At autopsy in cases of this kind we find the bile ducts permeable while the contents of the intestine are bile-stained. In certain other cases in which there is very intense and more or less long-continued jaundice the patients have bilious vomiting, but in spite of that the stools may be colorless (Lebert). In certain very grave cases of relapsing fever, on the other hand, icterus may be wanting entirely.

Among the disorders of the digestive organs we may mention first the anorexia occurring during the febrile paroxysm which disappears in the apyretic period. Sometimes indigestion and gastric catarrh occur and are prolonged into convalescence. In some exceptional cases the patients experience hunger throughout the entire course of the fever. We have already spoken above, in the general description of the disease, of the thirst which troubles the patient during the febrile stage and disappears in the period of apyrexia. During the attack the tongue is ordinarily coated with a whitish fur and is usually moist, but sometimes it is dry and covered with a yellowish or dark-yellow coating; very rarely it is cracked. The breath is often fetid. The patients complain of a bad taste in the mouth, of a dry, burning sensation in the pharynx, and sometimes of dysphagia. The region of the stomach is sometimes painful on pressure. Nausea and vomiting of a greenish or yellowish matter may be quite frequent during the early days of the disease, but most commonly cease later, and reappear only upon the approach of the crisis. In the grave forms of relapsing fever we may have hæmatemesis.

The action of the bowels is irregular, the patients sometimes complaining of constipation, at other times of diarrhœa. Occasionally during the crisis we observe a profuse diarrhœa, which takes the place of the ordinary sweating. Certain epidemics are characterized by profuse diarrhœa, with stools of a dark-yellow color; sometimes they are dysenteric in character and in such cases the disease is more

severe. Meteorism and pain on pressure over the abdomen are not rare. Involuntary discharges from the bowels are not common, occurring only in grave cases.

Nervous and Muscular Systems.—Cephalalgia torments the patient from the very onset of the disease, and during all the paroxysms. It ceases or diminishes only during the period of apyrexia. The patient also suffers greatly from vertigo, which, independently of the fever, forces him to keep to his bed from the first days of the disease. The nights are restless because of the pain and fever. In certain patients we find hyperæsthesia of sight and hearing. In most cases consciousness is preserved, delirium is quite rare. Douglas noted the occurrence of delirium in eight per cent. of his cases, and Murchison in two per cent.; it was usually quiet, but was sometimes noisy and occasionally was suicidal in character. Somnolence and stupor occur only exceptionally.

The muscular pains are very characteristic in relapsing fever. Coming on at the invasion of the disease, they are very violent from the start, especially in the lower extremities (calves of the legs). The lumbar and sacral regions are quite painful, especially at the beginning. The muscles of the neck, of the chest, and of the abdomen are also sometimes painful, but the pain here is less intense and of shorter duration. These pains become aggravated from time to time, and also wander from place to place. Often they are felt as the painful sensations of extreme lassitude. We also occasionally note the existence of pain in the articulations, which are, however, not swollen. Although these pains are very frequent, we might even say constant, their intensity varies in different epidemics, being sometimes very pronounced, at other times comparatively insignificant. They are felt chiefly during the febrile paroxysms, do not persist long after the beginning of the period of apyrexia, and disappear completely when convalescence sets in, leaving behind them, however, for quite a time a general debility of the muscular system.

Sometimes we find neuralgia limited to the shoulders, to the intercostal spaces, or to the hypogastrium. Certain patients, especially women, often complain of hyperæsthesia of the skin, which is sometimes quite pronounced. Ribalkin has observed during a paroxysm exaggeration of the tactile, as well as of the electrical and of the pain sense, while the thermic sensibility was diminished. The fall in temperature is followed by a diminution of all forms of sensation with the exception of the thermic sense, which rises as the temperature of the body falls.

According to Roudenko the tendon reflexes may be exaggerated, especially in cases marked by general excitement of the nervous sys-

tem, and may be diminished when this latter is depressed. Very commonly, however, the tendon reflexes show no deviations from the normal. In certain rare cases local anæsthesia of limited areas of the skin of the chest has been noted. We sometimes find deafness or ringing in the ears and, very rarely, hemeralopia.

Other nervous troubles occurring in the course of relapsing fever will be discussed in the section on complications.

Skin.—Notwithstanding the high temperature, the skin of patients suffering from relapsing fever does not feel so hot as in other of the typhoidal diseases, because it is always more moist than in these affections. Its color is frequently of a yellowish-gray tint, even when there is no pronounced icterus. Roseola is of rare occurrence and is never very marked. In those cases in which an epidemic of relapsing fever occurs at the same time with one of typhus fever an intense roseola (Cormac, Dümler) is frequently seen in those suffering from relapsing fever, but in these cases there may be a coexistence of the two infections. In certain epidemics, for example in St. Petersburg in 1864 and in Warsaw in 1881–83, a slight petechial eruption has been observed, especially on the skin of the hypogastrium and occasionally on the extremities, in which case it is usually seen on the feet and hands more particularly. Sometimes we note the occurrence of erythema and of bluish-red patches, which do not disappear on pressure. Sometimes during the critical sweat an abundant miliary eruption (sudamina) has been noted, occasionally leading to confusion with miliary fever. Finally, it is not uncommon to observe facial herpes (nasal, labial, auricular), which is almost never seen in typhoid or typhus fever. In certain epidemics urticaria has been observed in rare cases. During convalescence there is sometimes a quite pronounced desquamation of the skin.

Urine.—The condition of the urine in relapsing fever is interesting in view of the peculiarities of a disease which is divided into two periods so distinct as those of fever and of apyrexia. It might be supposed that the different febrile paroxysms would resemble each other as regards the condition of the urine, and that the apyrexial periods would also resemble each other in this respect. However, the changes which take place in the organism during the paroxysms and the fever-free intervals, leaving aside other factors, cannot but have a certain more lasting influence upon a secretion such as the urine; under the influence of the infection the chemism of the blood and of the tissues, as well as their morphology and their very structure, undergo periodically considerable modifications. It is for this reason that the examination of the urine in the different periods of the disease, and even at different days of the same period, is particu-

larly interesting. Unfortunately, however, we have few definite facts bearing upon this point. The period of incubation of relapsing fever ordinarily escapes observation because of the late entrance of the patients into the hospital, and the same is true of the first days of actual disease. During the paroxysms the urine has a general febrile appearance, but also presents certain peculiarities. It is secreted in small amount, high colored, of increased specific gravity, very acid in reaction, and readily becomes turbid and deposits a sediment. The quantity of urine excreted is generally markedly diminished during the febrile paroxysm, falling to 500 or 400 c.c. or even less. The smallest quantities are observed as the crisis approaches, often on the day of the critical sweat. During the apyrexial period the quantity of urine excreted reaches the normal, or even exceeds it. This occurs sometimes on the first or second day after the crisis, but more commonly during the second half of the fever-free period. The sweating and diarrhœa, which are common during the first days following the crisis, and also the general condition of the patient and the state of his heart, exercise a considerable influence on the quantity of urine secreted.

As regards the influence of temperature, we may note that there is not invariably a complete parallelism between the height of the fever and the degree of diminution of the urine. It is not uncommon to note at the beginning of the second and third paroxysms that the amount of urine excreted does not diminish as the temperature rises, but remains the same as during the preceding fever-free days or even rises slightly above the normal. In such cases the secretion of urine does not begin to diminish until after the fever has existed for some time, reaching its lowest point on the day before or sometimes on the very day of the crisis. Přibram and Robichek have noted a marked diuresis at the beginning of the primary attack in which there was intense fever. The occurrence of diuresis at the beginning of the febrile process would seem to denote renal congestion and an exaggerated secretory activity of the kidney. This fact of diuresis at the beginning of the febrile paroxysm or in general during slight and temporary elevations of temperature would seem to belong to the category of those which we have several times observed in different patients, and among others in those suffering from diabetes. In this disease when the temperature rises a little above the normal or during the early stages of some acute intercurrent febrile disease, such as typhoid fever for example, we often observe an increase in the amount of urine excreted, a diminution occurring only during the later stages of the fever. Such an increase in the secretion of urine upon the approach of the febrile paroxysm has also been observed by

Pasternatsky in a case of relapsing fever complicated with albuminuria and generalized œdema.

The quantity of urine ordinarily diminishes in the second and third paroxysms, just as in the first attack, during the height of the fever immediately preceding the occurrence of the crisis. It increases very slightly upon the day of the crisis, but more rapidly during the following days. It is also increased during convalescence and sometimes may become quite excessive, reaching 3,000, 4,000, or even 6,000 c.c. Increase in the secretion of urine throughout the second attack is noted only in rare cases.

The specific gravity follows in most cases the general rule that, when the amount excreted is small, as during the fever and especially in the primary paroxysm, the specific gravity is increased, and *vice versa.* However, we meet with notable exceptions to this rule, as an example of which I may relate the following: A patient had on the first day of the second paroxysm (with a temperature of 36.4° to 38° C.—97.5° to 100.4° F.) an excretion of 1,700 c.c. of urine of a specific gravity of 1.011; on the second day (with a temperature of 39° to 40° C.—102.2° to 104° F.), an excretion of 2,400 c.c. of a specific gravity of 1.012; on the third day (with a temperature of 39.7° to 40.4° C.—103.5° to 105.7° F.), an excretion of 1,400 c.c. of a specific gravity of 1.014; on the fourth day (with a temperature of 39.6° to 40° C.—103.3° to 104° F.), an excretion of 400 c.c. of a specific gravity of 1.011; on the fifth day (with a temperature of 39.7° to 40.1° C.—103.5° to 104.2° F.), an excretion of 600 c.c. of a specific gravity of 1.011; on the sixth day (with a temperature of 36.5° to 35.4° C.—97.7° to 95.7° F.), an excretion of 750 c.c. of a specific gravity of 1.010. The following day—that is to say, the second day of the second apyrexial period—the morning and evening temperatures were 35.4° and 37.5° C. (95.7° and 99.5° F.), the amount of urine excreted was 800 c.c., and its specific gravity was 1.010. This case presents a good instance of the very characteristic oscillations in the quantity of urine which often occur during the course of the second paroxysm, or first relapse.

The excretion of the solid elements in the urine is in relation with the quantity and specific gravity of this fluid, and like them varies within rather wide limits. The quantity of urea excreted during the presence of the fever is quite considerable, and may be above the normal, reaching 45 gm. or more in the twenty-four hours. This occurs especially during the course of the primary attack; in the subsequent paroxysms the increase in the excretion of urea is less constant, but it still occurs quite frequently, the oscillations being especially noticeable at the beginning and at the termination of an attack. Wyss and Bock have noted the following variation in the amount of urea excreted

during the twenty-four hours, the quantity being expressed in grams per kilo of the body weight: In the first paroxysm, 0.7737; in the first apyretic interval, 0.6631; in the second paroxysm, 0.8552; in the following fever-free period, 0.6169. Sometimes the reverse of this is observed, that is to say, there is a comparatively slight amount of urea excreted during the febrile attack, this being sometimes even below the normal, especially as the crisis approaches; during the period of apyrexia, however, at the very moment of the crisis or more commonly on the following day, the amount excreted rises to 50 or 60 gm. This is known as the critical or postcritical hyperexcretion of urea. Sometimes again an increase in the secretion occurs a little before the crisis—precritical hyperexcretion. A series of observations made in my service has shown that at the beginning of the second paroxysm or before it the excretion of urea may be relatively increased, this often coinciding with an increased excretion of urine.

The amount of chlorides in the urine is more constant than that of urea. Ordinarily, during the fever and the crisis the quantity of chlorides is notably diminished, falling sometimes to only a few decigrams in the day, just as it does in croupous pneumonia. In the period of apyrexia and during convalescence the amount of chlorides becomes again normal.

The variation in the amount of phosphates excreted is up to a certain extent parallel with that of the urea. In some cases we find an excretion of from 5 to 7 gm. during the twenty-four hours in the first paroxysm and the succeeding crisis. Robichek and Přibram found a reduction in the excretion of phosphates, as well as in that of sulphates. Hallervorden found, on the other hand, an increase in the amount of sulphates excreted, and also in that of ammonia. The amount of uric acid in the urine during the febrile paroxysm is sometimes greater, sometimes less than it is in the apyrexial interval.

It is not rare to find traces of albumin in the urine, but the frequency of albuminuria differs in different epidemics, being sometimes found in one-third of the cases (epidemic of 1868 in Prague) and sometimes in almost every case (epidemic of 1868 in Breslau and Berlin). Sometimes we find nucleoalbumin in the urine.

On microscopical examination of the sediment we find urates, crystals of uric acid, of oxalate of lime, and of triple phosphates, and a certain number of round cells, epithelial cells, and hyaline, epithelial (especially in the first paroxysm), and granular (especially in the second and following paroxysms) casts. The casts disappear when convalescence sets in. When relapsing fever is complicated by nephritis the changes in the urine are more marked and of longer duration. When icterus occurs we usually find bile pigments and the

biliary acids in the urine, and in the icteric forms of relapsing fever the urinary changes due to nephritis are often very pronounced, and we not uncommonly find blood in the urine. At other times we find evidences of catarrh of the urinary passages, renal pelves, ureters, and bladder, and also the associated vesical symptoms, such as dysuria, involuntary micturition, and sometimes hemorrhage.

When relapsing fever occurs as a complication of some other affection, we often observe changes in the quantity and composition of the urine. In the case of diabetes, for example, it is not uncommon to observe a diminution, or even absence, of glycosuria during the febrile paroxysm (Semon) as well as a reduced excretion of urine. But this is not an invariable rule, and I have personally observed a case of this nature in which the relapsing fever exerted no appreciable influence upon the course of the diabetes.

The *weight of the body* ought naturally to show marked oscillations in a disease such as relapsing fever. The fever, the anorexia, the insufficient alimentation during the paroxysm, the vomiting, and the diarrhœa all tend to diminish the weight of the body. This loss in weight often occurs with considerable rapidity. During the fever-free periods, however, the gain is usually quite marked. The loss in weight varies at different periods of the disease, and even during the several days of each period. While, during the febrile paroxysm the weight of the patient ordinarily diminishes by from 200 to 500 gm. each day, on the day of the crisis the loss is much greater, often from 1,200 to 2,800 gm., amounting sometimes to one-twentieth of the patient's normal weight. In the cases which I have studied in this respect the loss in weight was often greater during the crisis following the first paroxysm than in the subsequent ones, but of the latter it was usually greater after the third than after the second. The total loss of weight during the entire attack may amount to from one-tenth to one-fifth of the patient's normal weight. During the period of apyrexia, often within a day following the crisis, the patient begins to increase in weight, and continues to gain until the relapse appears. According to my observations the patient increases in weight after the second and third paroxysms, often from the day following the crisis, while in the first cycle of the malady the patient continues to lose weight on the day which follows the crisis. An exaggerated excretion of water and of the products of disassimilation, which takes place during the crisis, is, without doubt, one of the chief causes for the loss in weight at this time.

Blood Changes.—The most characteristic phenomenon of relapsing fever is, without doubt, the presence of spirochætæ in the blood. We have already discussed this point and the related facts of the bacteri-

cidal power of the blood of patients suffering from this disease, and of the immunity which is produced by inoculation with it, and we shall return to this latter question again. We shall here discuss certain other changes in the blood which have not been previously studied. The results of investigations by different authors concerning the general properties of the blood are not always uniform. Several of the earlier writers have noted that the venous blood was of a bright red color during the paroxysm (Christison) and almost always formed a clot, which would certainly indicate a different condition from that found in the other typhoidal diseases. Zorn and some other writers found that the blood drawn during the fever was of a tarry black color and coagulated slowly. During the apyrexia the blood was fluid and coagulated still more slowly. This difference in the experiences of different observers may be explained in part by the fact that the specimens of blood examined were taken from persons dying at different periods of the disease, and in part by the presence of complications which might modify the constitution of the blood. Motchoutkovsky asserted on purely theoretical grounds that the blood was of greater consistence during the crisis, but this opinion is not supported by facts. N. Traugott, analyzing the blood of living patients, found that its density usually diminished progressively during the course of the febrile paroxysm and especially after the crisis. During the period of apyrexia the density of the blood was rapidly increased in certain cases, while in others it remained slight. During the sweating stage a temporary increase in density was noted.

As regards the morphology of the red globules, these elements are not ordinarily changed to any extent. The number of red globules and the amount of hæmoglobin are reduced during the paroxysm (Chegloff) and are increased usually during the apyrexial period (although during the first days of this period the diminution continues), but during the following attacks again the diminution becomes progressive. Chegloff found a diminution in the amount of hæmoglobin and in the number of the red blood globules, but he could not discover any complete parallelism between these two phenomena. As a general rule the amount of hæmoglobin, and especially of oxyhæmoglobin, diminishes during the course of the febrile paroxysm, increases on the day of the crisis or the following day, and becomes normal during the apyretic interval. The same investigator found also that the hæmoglobin varies not only in quantity but in quality. We may find methæmoglobin in the blood, and the quantity of reduced hæmoglobin rises from 5.52 to 26.71 per cent. of the total hæmoglobin. Koudrine, in his investigations made in my clinic, found that the hæmoglobin is diminished in most cases during the

course of the fever, and increases to the normal during the period of apyrexia. But he found some exceptions to this rule. As regards the variations in the number of the red cells, he found that they followed in a general way those in the amount of hæmoglobin, although the two were not always exactly parallel. The reëstablishment of the hæmoglobin and red blood cells to the normal figure occurs much more slowly during the second apyretic period. We may add that Ianovsky, in treating the blood with a solution of sodium chloride, found that the resistance of the red blood globules to destructive influences had a definite relation to the degree of temperature, the resistance being greater during the pyrexia than in the fever-free period in which it is markedly diminished.

The white blood cells are notably increased in number. Cormac had referred to this, according to Allen Thompson who himself was the first to determine the fact of a considerable increase in the number of the white cells, not only during the height of the disease but in one case even before the attack had actually begun. Lapchinsky was, however, the first to make a count of the red and white cells in relapsing fever. He found, during the febrile paroxysm and immediately after the crisis, that the proportion of leucocytes was markedly increased. According to Heidenreich, the ratio of the white to the red blood cells in relapsing fever may be, in different cases, 1:80, 1:40, 1:30, or 1:20, and in one instance he found the ratio was 1:9. Koudrine also found the leucocytes increased in number in many cases. Their number ordinarily diminishes after the crisis, but sometimes they are at their maximum during the first few days of the period of apyrexia. During the febrile period, if this is not the final one, the number of leucocytes is greatest in the first days and then falls; but if it is the last paroxysm we find the number increasing during the attack and reaching its maximum in the closing days.

Ouskoff found an increase in the number of polynuclear neutrophiles (the over-mature elements, according to his classification) towards the end of the paroxysm, while after the crisis the number of these elements was reduced at the same time that the mononuclear leucocytes and the lymphocytes (the young elements, according to his classification) increased. Koudrine confirmed these observations of Ouskoff, and he also discovered that relatively the number of eosinophiles was diminished in very many cases during the febrile paroxysm. The same fact has been noticed by Schwarze, not only in relapsing fever but also in all forms of acute leucocytosis.

During the final days of the febrile paroxysm, and especially on the day immediately following the crisis, we find more or less constantly in the blood of patients suffering from relapsing fever large

protoplasmic bodies resembling leucocytes, but of much greater size. They have a diameter of 20 to 30 or even 60 μ, while that of the white blood cells is only from 9 to 12 μ, but between them and the leucocytes we find many intermediate forms. These bodies often contain a large number of round fatty granules and even fine fat drops, giving to them a granular appearance. We also find in them occasionally red blood cells and vacuoles.

In addition we find in the blood in relapsing fever very minute granules, either isolated or joined by fine filaments, sometimes resembling pneumococci, which have ordinarily very rapid movements. They differ from small fatty granules by their feeble refractive power, by their pale dull appearance, and by their ready staining with methylene blue. We know that Max Schultze has seen these formations in the normal blood, and others have found them in certain diseases other than relapsing fever, but there still remains the question of identity of the bodies discovered by different observers under different conditions. Some authors have thought they were specially numerous just before the beginning of a paroxysm of relapsing fever, and have been led by this to regard them as possibly the spores of the spirochætæ (von Jaksch, Sarnow), but this is a simple hypothesis which has not been proven. The protoplasmic formations just mentioned and these little granules sometimes form considerable masses, of a diameter of perhaps 92 μ, sufficient to occlude the capillary vessels.

Finally we also find in the blood free endothelial cells from the lining membrane of the vessels, which have usually undergone in part a fatty degeneration. The abnormal elements in the blood, which we have just mentioned and which have been described by Obermeier, Bliesener, Engel, Litten, Ponfick, Lapchinsky, Heidenreich, Guttmann, and others, are encountered usually towards the end of the paroxysm and especially immediately after the crisis, and they doubtless indicate that there exist at certain periods of the malady which we are now studying very considerable disturbances of the hæmatopoietic organs. But these elements cannot be regarded as specific for relapsing fever, since they are met with also in other diseases, such as typhoid and typhus fevers, measles, scarlet fever, diphtheria, intermittent fever, pericarditis, peritonitis, etc., and even in the normal blood. That which is characteristic of relapsing fever is the early agglomeration of these elements in rather large quantities and at definite periods of the disease. The supposition that these abnormal elements are formed in the spleen and are expelled from it at the termination of the febrile paroxysm is a plausible one, but up to the present time it lacks confirmation.

Complications.

The complications which may intervene in the course of relapsing fever are of varied character and origin. Some are very intimately and essentially associated with the primary disease and are a consequence of the specific infection, while others are foreign in their causation to the infection of relapsing fever and constitute idiopathic affections. Some of the latter are purely accidental and present their own individual symptoms, while others are the result of external influences, related to the infection of relapsing fever, and acting at the same time as the latter. The frequency of the complications of relapsing fever and their nature vary according to different epidemics. Thus in certain epidemics the infection is more grave and is followed by a great number of complications, while in others the disease is as a rule mild in character and the number of complications is small.

As regards the general and individual conditions which predispose to the intercurrence of complications we may remark that the latter are more common in women, both in those who die and in those who recover, than they are in men. Thus, according to Jogikhess, 384 out of 1,001 men who recovered had suffered from complications (38.26 per cent.), while in women the proportion of complications was about 40.5 per cent. The same difference was noted in the cases which terminated fatally: in men complications were noted in 91.43 per cent., but in women in 94.12 per cent.

There is no special time in the course of relapsing fever which seems more favorable than another for the development of complications, for they appear to have no relation with the febrile paroxysms, developing at all periods of the disease. We can only say in this respect that the period at which complications are most frequent is that which most often terminates in the death of the patient. We shall speak of the effect of the complications upon the prognosis in a later section.

We need not occupy ourselves here with the individual accidental complications. We would only note that, in examining the records of various epidemics, we find that certain chronic maladies which are of quite frequent occurrence are very seldom encountered in patients suffering from an attack of relapsing fever, while other less common chronic diseases are observed with more than ordinary frequency in these individuals. In the observations of Borkhsenius, for example, in 522 cured cases of relapsing fever we find not one of chronic endocarditis, while chronic pneumonia was noted in the previous history of 7 cases. The same is true, moreover, in respect of complications with certain acute inflammatory affections of

certain organs, for some are frequent while others are relatively rare. In the report of the Barracks Hospital at St. Petersburg for ten years, comprising three epidemics with 3,315 cases, we find a complication with croupous pneumonia alone in 17 cases out of 145 deaths, not to speak of other acute and chronic forms of pneumonia. Only one case of chronic endocarditis and two cases of chronic pericarditis have been reported. We find no mention in the two reports above quoted of acute endocarditis occurring as a complication of relapsing fever. Griesinger states that one of the older authors reports one case of this kind. The heart muscle is very often affected, as we have seen above when speaking of the syncopal form of relapsing fever, and as we shall see again in a later section.

Among the diseases which develop at the same time as relapsing fever we may first mention those of which we have already spoken briefly above, namely, typhus, typhoid, and intermittent fevers, and following these diphtheria, smallpox, pyæmia, erysipelas, hemorrhagic meningitis, and often acute catarrhal or still more frequently croupous pneumonia.

In certain epidemics *pneumonia* is a frequent complication and may influence more or less the outcome of the disease, increasing the death rate. According to the observations of Lebert, pneumonia occurs ordinarily during the primary paroxysm or else in the first relapse. It is usually in these cases double. In mild cases the pneumonia commonly ends in resolution, but in severe cases, and especially in alcoholic patients, it results in death. According to the observations of Ouskoff, the most frequent complication in the epidemics which prevailed in St. Petersburg from 1882 to 1887 was croupous pneumonia, in 31 per cent., and following that dysentery, in 18.1 per cent. While according to the observations of the same author, in the idiopathic form of croupous pneumonia the right lung is affected more than twice as frequently as the left, the pneumonia complicating relapsing fever shows a decided preference for the left lung.

For observations bearing upon the complication of relapsing fever by *typhus and typhoid fevers* we are indebted especially to Russian physicians (Botkin, Borodoulin, Shtchastny, and others). It is evident that these affections developing simultaneously in the same individual (a somewhat rare occurrence) would be manifested by the clinical and anatomico-pathological phenomena belonging to one and the other of these typhoidal diseases. The presence of spirochætæ in the blood, leaving aside the other more or less characteristic symptoms, is an element of decisive diagnostic importance as regards relapsing fever, just as is for typhoid fever the presence of Eberth's

bacillus in the intestinal contents or in the blood. In one case in which the symptoms were mixed, Borodoulin found spirochætæ in the blood of the patient while living and the characteristic lesions of typhoid fever in the intestine after death. Another case is on record in which typhoid bacilli and spirochætæ were found in a culture of blood taken from the spleen (Ippa). In the case of typhus fever, unfortunately, we have no certain diagnostic sign other than the ordinary clinical picture of the disease. Among the usual symptoms the more or less abundant exanthem plays an important rôle, but we are unable as yet to discover any characteristic and specific microorganism. Salomon has reported a case of typhus fever combined with relapsing fever in which the presence was noted of spirilla in the blood. There is no definite period for the occurrence of the complication of one with the other disease, for in some cases one, in others another is the primary affection. As we have already said, however, typhus fever more often follows relapsing fever than precedes it, and the same is apparently true of typhoid fever when coexisting with relapsing fever. The combination of relapsing fever with typhus or typhoid fever would seem, according to Botkin and certain other writers, to mitigate the severity of the symptoms of each disease. The course of each disease is much more favorable and the mortality is lower than when typhoid or typhus fever develops alone and uncomplicated by relapsing fever. But this statement requires confirmation, for cases in which relapsing fever is certainly coexistent with either typhus or typhoid fever are quite rare; and furthermore, this rule was formulated at a time when the diagnosis of a combination of this sort was based chiefly upon some irregularity in the temperature curve or on the appearance of an eruption or some other equally indefinite indication.

As regards the coexistence of relapsing fever and *intermittent fever*, we have not only instances recorded by the older observers at a time when bacteriology did not exist, but also recent observations in which all the modern methods of research were used. A case has been reported of intermittent fever complicated by relapsing fever in which there were found in the blood not only the spirochætæ of typhus recurrens, but also the plasmodia of malaria. The malaria had produced a modification of the temperature curve of relapsing fever, causing very marked oscillations in the course of the day (remissions) and the termination of the paroxysms by lysis. Mamourovsky also found in the blood of a patient with relapsing fever of clearly remittent type spirochætæ as well as the plasmodia of malaria. After the administration of quinine (0.75 gm. = gr. xii.) the fever became continuous and spirochætæ alone were found in the blood, and these also

disappeared when the temperature fell to normal. The second paroxysm of the relapsing fever occurred two weeks later and lasted a little more than twenty-four hours, spirochætæ being found in the blood. Two weeks later there were two paroxysms of quotidian intermittent fever, and at this time plasmodia were again found in the blood and finally disappeared only after the administration of 1.2 gm. (gr. xviii.) of quinine.

Diphtheria may complicate relapsing fever at any of its stages, but most frequently, it would appear, after the first or the second crisis. Lipsky has reported a case of relapsing fever complicated by pharyngeal diphtheria appearing after the second crisis; the patient had a third paroxysm while the diphtheria was still present, but the disease terminated in recovery.

Brajnikoff has described a case of relapsing fever complicated with *smallpox*. After the third paroxysm of relapsing fever, the temperature being 40° C. (104° F.), the eruption of smallpox pustules appeared. Examination of the blood showed the presence of the spirochætæ of relapsing fever.

In addition to the complications already mentioned I have seen one in the case of a workman twenty-two years old, in whom *measles* appeared on the ninth day of the period of apyrexia following the first paroxysm. The measles developed as an independent affection rather than as a complication. The patient recovered.

Pyæmia may occur at any period of the disease, but commonly follows the paroxysms.

Among the other complications of a more or less general character *scurvy* is worthy of attention. It may precede relapsing fever, develop in the course of this disease, or follow it. Borkhsenius observed in the epidemic of 1880 at St. Petersburg 24 cases of scorbutic complications out of 522 cases of relapsing fever. In most of these cases scurvy was the primary affection, but in some the scorbutic symptoms appeared after the first or second febrile paroxysm of relapsing fever. Out of 24 patients 2 died, giving a mortality of 8.03 per cent. (The general mortality in this hospital was 6.1 per cent.) In these cases the duration of the relapsing fever was longer than usual, due principally to the great number of paroxysms, but also to the longer duration of each paroxysm and of the succeeding interval. The fever was for the most part of a frankly remittent type, while in the other non-complicated cases it was nearly continuous.

As regards the diseases of various organs which may complicate the course of relapsing fever, we may say that they are not very infrequent. On the part of the *nervous system* we observe during and after the fever, as well as during convalescence, though not very often, various troubles, such as delirium, convulsions, sometimes of an epilep-

tiform character, trismus, stiffness of the neck muscles, and loss of consciousness. Among the nervous symptoms we might also mention involuntary movements from the bowels, retention of urine, etc. All these phenomena are observed most frequently during the febrile paroxysm and are not always due to meningitis, which occasionally complicates these cases, chiefly under the form of pachymeningitis. Paralysis is observed in rare cases, and still more rarely aphasia. The paralysis appears sometimes under the form of hemiplegia and of paraplegia (even of the four extremities, as in a case reported by S. S. Parry), and sometimes in the form of isolated affections of various members, of the rectum, etc., or of certain nerves. These alterations may be of central, but more frequently are of peripheral origin. The resultant conditions may be purely functional or associated with actual lesions of degenerative or inflammatory character. Organic lesions are, however, comparatively rare, and it is for this reason that the paralyses which develop usually, but not invariably, during or after the second crisis are for the most part of relatively short duration, seldom being permanent. We sometimes observe disturbances of sensation, such as neuralgia or anæsthesia. The various anæsthesias, as well as motor paralyses, may be localized or more or less diffused. General anæsthesia of the skin has been recorded but once. The anæsthesia may exist coincidently with motor paralysis or independently of it. It may involve all forms of sensation or only one or more. These anæsthesias and paralyses are usually only temporary, lasting for from a day or two up to two weeks, but purely localized troubles of this sort may last a long time, and sometimes for life. We have already mentioned the occurrence of pachymeningitis as a complication. According to Kremyansky it is met with more frequently in those addicted to alcoholic abuse. Occasionally purulent meningitis has been observed. In a few cases mental troubles have been noted among the sequelæ.

The *eye* is often the seat of various pathological processes. We often note ecchymoses of the conjunctiva, phlyctenulæ (Litten), conjunctivitis, hypopyon, keratitis, descemetitis (the formation of fine granulations on the posterior surface of the cornea), iritis, iridocyclitis, iridochoroiditis, and opacity of the crystalline; these troubles usually terminate in recovery. Other affections that have been noted are retinal hemorrhage, optic neuritis, temporary amaurosis, and paralyses of accommodation and of the ocular muscles, troubles resulting from embolism, inflammatory changes of the nervous or muscular elements, degenerative changes, etc. Dolgenkoff has reported a case of diffuse retinitis with symptoms of multiple sclerosis occurring as sequelæ of relapsing fever.

We sometimes also find *ear* troubles due to catarrhal inflammation of the tympanum or sometimes to suppuration of the middle ear with perforation of the drum membrane. Pharyngitis as a cause of these lesions is, however, not of frequent occurrence. Sometimes we meet with functional troubles of hearing of a very peculiar character. Meschede, for example, observed in his own person the occurrence of a peculiar, weak, but very distinct noise in the left ear when some one blew upon the upper part of the pavilion of the right ear.

Among other occasional complications we note swelling and inflammatory changes of the *lymph bodies* (submaxillary, occipital, or inguinal), and also of the *salivary glands* (parotid and submaxillary), with a tendency to suppuration. We also note pharyngitis and cellulitis of the neck as well as laryngitis, terminating perhaps in abscess or œdema of the glottis. In isolated instances there have been noted stomatitis, angina, swelling of the lingual glands, necrotic changes in the mucous membrane of the larynx and bronchi, and sometimes ulceration of the posterior wall of the larynx, such as have been observed in typhoid fever.

Among other affections of the respiratory organs is sometimes noted intense *bronchitis*. Various inflammatory processes in the lungs are not uncommon; usually they are of lobular localization and widely disseminated, showing a tendency to coalesce and form diffuse areas of consolidation. A quite frequent complication of relapsing fever is croupous pneumonia, of which we have already spoken. We may add, however, that the pneumonia is frequently associated with a serofibrinous exudation in the pleura. The pneumonia may end in suppuration and be followed by death. Sometimes we find in the lungs infarcts which may result in gangrene, perforation of the pleura, and pyothorax ending in death. Dry pleurisy or pleurisy with effusion may also be observed as a complication of relapsing fever independent of the occurrence of pneumonia, and in such cases it usually terminates favorably. We sometimes find also indications of a possible complication with pleural or pulmonary tuberculosis.

Complications on the part of the *serous membranes*, such as pleurisy, pericarditis, endocarditis, or peritonitis, are very rare in relapsing fever.

As regards the *digestive organs*, beyond the frequent troubles of which we have already spoken (anorexia, nausea, vomiting, etc.), we sometimes find hæmatemesis in grave cases. The constipation which is very common at the beginning of the fever frequently gives place later to a diarrhœa. Among other intestinal complications we may mention follicular enteritis, intestinal hemorrhage, and dysen-

tery, with diphtheritic processes in the lower part of the ileum and more rarely in the large intestine.

Of the *hepatic* and *biliary* complications we have already discussed icterus and that grave form accompanied by jaundice which Griesinger called bilious typhoid and described as a special form of relapsing fever. Other very rare hepatic complications are infarcts and cirrhosis of the liver.

The increase in volume of the *spleen*, which sometimes reaches excessive proportions in relapsing fever, may lead to rupture of the organ and fatal hemorrhage. Abscess of the spleen may result from infarction. Sometimes the presence of an abscess of this sort will be declared by hectic fever, chills, night sweats, local pain in the hypertrophied spleen, and adynamia; at other times the symptoms are rather those of trouble in the neighboring organs, such as localized peritonitis, pleurisy of the left side, parapleuritis, etc.; in such cases the fever has a less hectic character, is not broken by such marked remissions, and is accompanied by fewer chills and less profuse sweating. In addition we may occasionally see perisplenitis, purulent inflammation of the ribs or diaphragm, bronchorrhœa, etc. As would naturally be supposed, these complications are terminated frequently by death, yet recovery is not by any means impossible.

Very severe acute *nephritis*, apart from the presence of traces of albumin and hyaline casts in the urine, already mentioned, is an occasional complication of relapsing fever; it comes on during the primary paroxysm or at a later stage of the disease, following the second febrile paroxysm, for example. Its presence is manifested by pains in the lumbar regions, a diminution in the excretion of urine, an increase of the albuminuria, the appearance of epithelial, hyaline, and other forms of casts, and occasionally blood containing spirochætæ in the urine. This form of nephritis rarely becomes chronic, but after a longer or shorter duration terminates in recovery, the patients rarely succumbing to uræmia. In one case reported by Borkhsenius, a patient, twenty-eight years of age, had nephritis with œdema following the second febrile paroxysm. This patient had five paroxysms, being fifty-four days in the hospital, but finally made a good recovery. Another patient, thirty years old, who was seized with nephritis in the primary paroxysm, left the hospital at the end of twenty-seven days completely cured.

Some patients complain of *rheumatoid pains* in the articulations, and occasionally we find on examination redness and swelling of the affected joints. The most frequent seat of these pseudo-rheumatic affections are, in the order of frequency, the upper extremities (fingers, wrists, elbows, shoulders), and then the knees; but this order may be

reversed. The character and the course of relapsing fever in which this complication is encountered do not differ in any respect from those of an uncomplicated case. The changes in the joints usually terminate in recovery, yielding readily to the action of salicylate of sodium.

The *genital organs* in women may be the seat of certain complications in the course of relapsing fever. Apart from abortion, of which mention has been made above, we sometimes see a sanguineous discharge simulating menstruation, or amenorrhœa (Bartel), hemorrhagic endometritis, and purulent ulcerative colpitis.

On the part of the *skin*, in addition to the affections already discussed (ecchymoses, erysipelas, etc.), we sometimes observe, though very rarely, the lesions of decubitus. Sometimes we see gangrene of the feet or other parts, as the nose, lips, etc., or septicopyæmia. Quite frequently we find among the secondary affections complicating relapsing fever abscesses in the cellular tissue and in the lymph bodies, sometimes also in the salivary glands (especially the parotids) and in other organs.

Sequelæ.

During convalescence certain patients suffer for quite a long time with anæmia, palpitations, pains in the extremities, and anasarca. Finally generalized œdema and ascites, albuminuria, thromboses in the blood-vessels, tuberculosis, diabetes, cirrhotic processes in the liver, and the various nervous and mental troubles of which we have spoken above (contractures, paralyses, deaf-mutism, amaurosis) have been recorded among the sequelæ of relapsing fever.

Pathological Anatomy.

It is very evident that, in an affection such as relapsing fever in which febrile paroxysms may alternate with apyretic intervals and in which the intensity of the infection may vary within very wide limits, and which may also be complicated by various other diseases, the pathological changes found post mortem, even those that are more or less constant and characteristic of relapsing fever, may vary considerably in their appearance and intensity. These characteristic lesions are, furthermore, not very numerous in relapsing fever.

The most characteristic change observed in this disease is the presence of spirochætæ in the blood. One would think that after death, at least in those who had died during the febrile paroxysm, the same pathognomonic pathological phenomenon would always be

met with. This is far from being the case, however, at least with the methods of research at present at our command, as regards the finding of spirochætæ. It was not so long ago that it was generally believed that the spirochætæ could not be found in the blood after death, but the researches of numerous investigators (Heidenreich, Albrecht, Lachmann, Lubimoff, Nikiforoff, and others) have shown that the microorganisms may occasionally be found in the blood, at least in that of the spleen. Of course they would not be found in the blood of those who had died in the period of apyrexia.

Other essential lesions are found in the spleen more especially, but also in the bone marrow and in the liver. The other parenchymatous organs (kidneys, muscles, lungs, etc.) participate more or less in the morbid process, just as they do in other infectious fevers. The following is a picture of the pathological changes ordinarily found after death from relapsing fever:

Rigor mortis appears early and persists for an unusually long time. The *skin* is often of a pale-yellow color, and sometimes we observe petechiæ and ecchymoses. In the bilious form of relapsing fever we find a very marked icteric discoloration of the skin and mucous membrane, as well as of the internal organs. Ordinarily general nutrition is but little affected.

The *muscles* are usually rather dry and of a dark-red color. Sometimes we find, as in typhus and typhoid fevers, hemorrhagic infarcts and spots of softening in certain muscles, especially in those of the abdomen. Microscopical examination of the muscular tissue shows granulofatty degeneration with proliferation of the nuclei of the muscular cells (L. Popoff). The small vessels which ramify in the muscular tissue also undergo marked alterations: the nuclei of the smooth muscular fibres of the arterioles are often increased in number and are in process of division. The vessel walls in their several layers, especially in the internal and middle coats, are infiltrated in places with small, young cellular elements. The endothelium of the vessels is often swollen and split up into several layers.

The *heart* muscle is often very pale, soft, flaccid, and of a dirty or grayish-yellow color. On microscopical examination the muscular fibres in these cases present evidences of a very marked granulofatty degeneration. The cells of the nervous ganglia of the heart are swollen, their protoplasm is cloudy and sometimes fatty degenerated, and their nuclei are indistinct or wholly invisible. The edges of the cells are irregularly indented. The vessels surrounding the ganglia are hyperæmic (Kouznetsoff, Poushkareff). The lesions of the cardiac muscles resemble those seen in diphtheria and other septicæmic or puerperal infections (Ponfick), and sudden death in collapse is a

not infrequent result of these changes; but of course extensive lesions of this nature are not found in every fatal case.

The mucous membrane of the *pharynx* and *larynx* often presents the lesions of catarrhal inflammation with slight swelling and redness. On the epiglottis and entrance of the larynx we find erosion, sometimes intense œdema, and ulceration, especially on the posterior wall, such as we see occasionally in typhoid fever. In very grave cases we find also fibrinous and diphtheritic membranes. The bronchial glands are swollen and congested. The mucous membrane of the *bronchi* is almost always the seat of a catarrhal inflammation with swelling, redness, and an abundant secretion. The *lungs* are often anæmic, but show no lesions peculiar to relapsing fever. Sometimes we find them the seat of a catarrhal inflammation (lobular pneumonia) with atelectasis and phenomena of hypostasis and œdema. Finally a rather frequent condition, especially in certain epidemics, is croupous pneumonia, of which we have spoken above in the section on complications.

Of all the organs the *spleen* presents the most constant and the most characteristic lesions. It is increased in size in all cases of relapsing fever, except those in which the subject has succumbed late in the course of the disease as a result of some complication. This increase in size is generally quite considerable, the dimensions of the spleen being sometimes five or six times the normal. Of all the so-called typhoidal affections it is precisely relapsing fever in which the increase in size of the spleen is most marked. Its weight in this disease sometimes reaches 2,235 gm. (about five pounds), according to Kuettner. The capsule of the spleen is ordinarily tense, smooth, and sometimes more or less opaque. Occasionally we see on it areas of recent fibrinoid deposits. The tension of the capsule is sometimes so great that the envelope is ruptured. The parenchyma of the organ is of a dark-red color and ordinarily very soft, sometimes indeed almost liquefied. It is hard only in those cases in which some chronic cirrhotic process has existed previously, leading to the formation of a large amount of new connective tissue. On section the surface is sometimes smooth, sometimes and more commonly the Malpighian corpuscles form quite distinct projections; the parenchyma is occasionally strongly pigmented in places. We often find on the cut surface a number of small, rounded, or irregular points of a dull-yellow color sometimes containing a collection of granular detritus in their centre. The hypertrophy of the spleen is due in great measure to hyperæmia with dilatation of the blood-vessels, and also to a quite considerable increase in the number of the cellular elements of the pulp, as well as of the lymphatic cells of the Malpighian corpuscles.

On account of the hyperæmia the vessels are gorged with blood and dilated. The proliferation of the cellular elements causes a compression of the vessels at certain points, and this leads to collateral congestion with blood stasis and degeneration of the elements. When the process of proliferation in the Malpighian corpuscles is very pronounced, as happens in the grave cases, especially in the form called bilious typhoid, the enlarged spleen is, according to the expression of Griesinger, sown with thousands of little grayish-yellow grains. These granulations, which are simply Malpighian corpuscles enlarged and increased in number, are at first hard and of the size of a hemp seed or poppy seed. Soon suppuration sets in so that the entire spleen looks as if it were riddled with numerous miliary abscesses, not confluent, and each containing a droplet of pus. These little abscesses are evidently the same as the minute points observed by Ponfick, to which he gave the name of arterial foci and which he thought were derived from the hyperplastic tissue of the follicles, the central elements of which had undergone granulofatty degeneration and disintegration. These foci occupy a large or a small area corresponding to the distribution of an artery, the walls of which also contain a number of fat granules, showing that the nutrition of the part is profoundly disturbed.

Lubimoff has noted the presence of spirochætæ in the Malpighian corpuscles and in the infarcts, and it is to the action of the micro-organisms that he attributes the lesions noted. Metchnikoff found spirochætæ in the spleen of monkeys which had been inoculated with relapsing fever, either at the height of the febrile process, just before the crisis, or later during the period of apyrexia. In preparations stained after Gunther's method, the spirochætæ were found for the most part in the polynuclear leucocytes. Nikiforoff found them, however, in the spleen of a person dead of relapsing fever, sometimes free and sometimes enclosed in degenerated cells.

In addition to these minute isolated collections we find very often (according to Ponfick in forty per cent. of all cases) larger formations in the spleen, infarcts, which on account of their frequency, their large size, and their various untoward consequences, are possessed of great importance and a special interest. These infarcts occur sometimes in the form of large, distinctly isolated, wedge-shaped collections, occasionally occupying two-thirds of the entire organ; they are found immediately beneath the capsule. Sometimes, however, they are of smaller size, rounded or irregular in outline, and are situated in the deeper portions of the spleen. When of recent formation, they are dark red in color, but with time they gradually change through reddish-gray and grayish-yellow to yellowish-white. Their surface on

section presents at first slightly projecting granulations, but as the changes just mentioned take place it assumes the flat and uniform appearance of any other caseous centre. They may be solid or in a state of softening and disintegration. Sometimes they are surrounded by a congestive zone, a sort of inflammatory reaction. In their evolution and course they greatly resemble the embolic infarcts which occur in the course of diseases of the heart, but they differ from the latter in that there is no endocarditis present and there are no emboli in the afferent arteries. Ordinarily we find thrombi in the corresponding veins (Ponfick, Poushkareff). Ponfick has described them under the name of venous infarcts. Their origin is indeed often very obscure and should be searched for with the greatest care. The proliferation and in general the other changes in the elements of the pulp, the vascular endothelium, the sinuses, etc., may perhaps possess a certain influence in this respect. The small foci, after undergoing necrotic changes, may be absorbed, leaving cicatrices. The large collections sometimes cause inflammation, suppuration, the formation of abscesses, perisplenitis, peritonitis, pleurisy, ulceration and perforation of the lungs, and sometimes rupture of the spleen with consequent fatal peritonitis. In some cases rupture of the spleen may be produced, as we have said before, without the occurrence of suppurating infarcts, but simply in consequence of the excessive enlargement of the organ, due to hyperæmia, which may cause the capsule to burst. Poushkareff, examining the spleen at different periods of relapsing fever, found that, as a rule, there was during the first attack considerable increase in the number of lymphoid elements, in part only in the Malpighian corpuscles, in part in isolated centres in the splenic pulp. In the first apyrexial period there is a regressive transformation (granulofatty degeneration) in these two kinds of lesions. In the second febrile paroxysm new centres appear between the preceding ones. In the second period of apyrexia these new centres undergo regressive transformation. During the third cycle of fever and consecutive apyrexia the same changes take place. This method of evolution of the splenic lesions would enable us, the author believes, to determine in which of the first two paroxysms the patient has died. In the first case we have centres of the first stage of evolution, and in the second the two generations which are easily distinguished. In the case of death taking place after the third and following paroxysms it is more difficult or even impossible to distinguish the lesions of different ages. The regressive transformations of the first and second paroxysms prevent us from distinguishing the lesions of the following paroxysms, and only the recently proliferated ganglia of the last attack are to be made out.

If there has been but one paroxysm we may readily determine whether death has taken place during the crisis or in the apyrexial period, provided the latter lasted more than five days. We ought, however, to mention that Fedoroff has found in patients dead at the end of the first paroxysm regressive transformation of the cellular elements in the central portion of the Malpighian corpuscles and the hemorrhagic infarcts in the spleen; this is in contradiction with the findings of Poushkareff, who found this regressive transformation only after the second paroxysm. To what we have said it is necessary to add that Nikiforoff and Fedoroff have noted the occurrence of hyaline degeneration of the vessels of the spleen.

In those who have died some time after the termination of the disease the increase in size of the spleen is less marked and the capsule is wrinkled.

The *liver* is usually notably affected in relapsing fever. It is increased in size to a considerable extent, often more than in any other acute infectious disease. The enlargement is chiefly of the left lobe. The liver is sometimes engorged with blood and firm in texture; at other times and more frequently it is anæmic, soft, and friable. We can sometimes see on its peritoneal investment a fresh fibrinous exudate in the form of a fine network or membrane. On section the cut surface is usually of a reddish-gray color, sometimes yellowish-gray or slate color. The boundaries of its lobules are indistinct. The increase in size of the liver results primarily from hyperæmia, especially in patients who have died during a febrile paroxysm. In such cases we often find the blood-vessels noticeably dilated, but during the period of apyrexia they become contracted. We usually find swelling and granular degeneration of the liver cells, often with increase in number of their nuclei. We also find more or less marked fatty infiltration of the peripheral zone of the lobules and sometimes even infiltration of small cells around the portal vessels and bile ducts. The first phenomenon is constant, the latter less so. The more febrile paroxysms there have been the more the vessels are dilated. The endothelium of the blood-vessels is often swollen and granular. If the relapsing fever is complicated with icterus, this latter condition is observed in the liver, especially in the central portions of the lobules, which are then of a more yellow or even greenish color. In such cases the hepatic cells in these parts contain granulations and bile pigment. We also find in some places a dilatation of the bile ducts, in others a swelling of their epithelium with exfoliation, leading to occlusion of the ducts. We also find the lesions of periangiocholitis and sometimes general proliferation of the connective tissue of the liver. In rare cases there are in the liver, as well as in the spleen,

the above-mentioned minute centres of softening with hollowing out of the central portions. Sometimes we find more or less extensive abscesses (Lubimoff). Some observers have noted in exceptional cases of icterus that the liver is flaccid and small after a prior period of enlargement. Under the microscope it shows the changes commonly observed in pernicious jaundice.

The gall-bladder is in most cases more or less filled with a pale yellow or brown bile.

The *kidneys* are usually increased in size, their weight in some cases being doubled. Sometimes they are hyperæmic, but more often anæmic. The cortex is thickened and pale in color and the pyramids are injected; or both cortex and medullary substance are of a grayish or pale-yellow color and friable. Usually the capsule is readily detached and rarely is adherent. Microscopical examination shows a more or less marked granular swelling and sometimes fatty degeneration of the epithelium of the urinary tubules. The interstitial tissue is also sometimes infiltrated with young cells. Poushkareff found glomerulonephritis, though not very marked, as an ordinary occurrence, and Fedoroff found inflammatory lesions of similar nature. The latter also observed the presence of very pronounced lesions of the epithelium of the convoluted tubules. The cells are in the form of triangular masses, separated from each other and raised from the underlying membrane. They are homogeneous and without trace of nucleus, so that the picture presented is one rather of necrosis (coagulation necrosis) than of simple granular degeneration. Such a transformation recalls the picture of the epithelial changes in the kidneys which I observed in the course of experiments to determine the effect of high temperatures on rabbits (*Virchow's Archiv*, Bd. 87, 1882). Other observers have found the lesions of hemorrhagic nephritis and have noted effusion of blood in Bowman's capsules and in the lower parts of the convoluted tubules and Henle's loops (Erichsen, Ponfick, Lubimoff). Sometimes we find in the kidneys cuneiform infarcts, for the most part in different stages of regressive metamorphosis. We find also abscesses in the cortical layer of the kidney, and quite commonly catarrhal lesions in the pelves.

The *stomach* and *small intestine* present evidences of catarrhal inflammation. The intestinal contents are stained with bile. We sometimes see on the mucous membrane of the stomach and intestine erosions and hemorrhagic effusions. The swelling of the solitary glands, Peyer's patches, and the retroperitoneal glands is rather rare, but little marked when present, and comparable in no sense to that observed in typhoid fever. We sometimes meet with diphtheritic and fibrinous inflammations, especially in the colon. There is often

a swelling of the mesenteric, gastric, splenic, renal, and retroperitoneal ganglia.

In the *bone marrow* Lubimoff, Ponfick, and others have found constant diffuse changes, for the most part microscopical, and also (according to Ponfick in thirty per cent. of all cases) certain areas, visible to the naked eye, of softening. The lesions first mentioned consist chiefly of fatty degeneration of the elements of the vascular walls, especially of those of the arterioles, and the aggregation in their external tunics of a great number of granular cells (Körnchenzellen) and fatty granules. These changes are sometimes so pronounced that we can distinguish the vessels macroscopically as white lines. The medullary tissue contains fine fatty granules, lymphoid elements, polynuclear cells, and cells containing red blood corpuscles. According to Poushkareff these changes in relapsing fever differ from those found in typhus and typhoid fevers, in that in the first there are always very many small fat granules and very few elements containing red blood corpuscles, while in the second the fatty granulations are scanty or wanting and the elements enclosing red blood cells are relatively numerous. The isolated lesions, sometimes small and sometimes attaining a considerable size, are simply fatty necrotic masses. Of foreign elements we find only a small number of granular cells and isolated pus globules, but no red blood corpuscles. The latter and the lymphoid elements are encountered only outside of these necrotic areas near their periphery. The diaphyses of the bones are hyperæmic (Poushkareff).

Brain and Cerebral Meninges.—In the meninges we may find various alterations. The lesions of hemorrhagic pachymeningitis are specially frequent. Out of forty-five cases Poushkareff found fifteen of internal pachymeningitis, and in eleven the pachymeningitis was hemorrhagic. The pia is anæmic, cloudy, and œdematous, and is sometimes the seat of hemorrhagic and inflammatory lesions. Suppurative inflammation is seen chiefly in cases complicated with otitis media or with croupous pneumonia. The cerebral cortex is often anæmic, but in rare instances its vessels are more or less filled with blood. Sometimes we find effusions of blood in the cortex as well as in the optic thalami and corpora striata. The hemorrhage occurs chiefly as minute red points in the cerebral tissue; sometimes it is more considerable. Abscess of the brain has rarely been noted.

In certain cases microscopical examination reveals no changes whatever, but in other cases we find lesions similar to those encountered in other typhoidal affections, and especially in typhoid fever (L. Popoff). Lubimoff says that in his observations, which referred to the icteric form of relapsing fever, the nervous elements of the cere-

bral substance presented various degrees of cloudy swelling. Some of the nerve cells were but faintly clouded and finely granular and their nuclei projected distinctly, while others were coarsely granular, sometimes without any trace of nuclei, and with indented outlines. Alongside of these two sorts of cells were intermediate forms. In addition to this there was around the blood-vessels of the white and the gray substance and also around the nervous elements in the pericellular spaces an accumulation of indifferent cells, especially pronounced in those cases in which abscess of the brain existed. The endothelium of the vessels showed at times lesions of a regressive character, at other times swelling of the protoplasm and multiplication of the nuclei. In teased preparations Lubimoff found in the protoplasm of the nerve cells the presence of indifferent cells, in number varying from one to three in each cell.

The same author found similar lesions in the *spinal cord*, although less marked, and in addition pigmented and hyaline degeneration of the nerve cells. The same lesions were also noted in the sympathetic ganglia. In the nerves (sciatic and cervical sympathetic), alongside of normal fibres were found others irregularly swollen, divided at unequal lengths, and homogeneous or granular in structure. In places the nerve fibres showed a thick granular layer, which on staining with osmic acid became of a dark gray to black color.

Diagnosis.

The course of relapsing fever is so characteristic that its diagnosis presents little difficulty, even in the early days of an epidemic, if all the modern methods of research are made use of in the examination of the patient. During the primary paroxysm there may be some doubts, but the very characteristic rapid and pronounced elevation of temperature, the equally rapid and pronounced increase in size of the spleen and of the liver, the tenderness in these organs and especially the pains in the muscles, and also the other peculiar symptoms of the disease, which we have described in detail in a previous section, enable us to distinguish relapsing fever without difficulty from other affections of a similar nature and appearance, such as typhus and typhoid fevers. Typhus fever with its rapid evolution is more likely than is typhoid fever to be confused with relapsing fever in the early stages of this malady. The invasion of typhoid fever is ordinarily slower and more progressive, with the exception of the abortive form which begins quite suddenly. But in any case the relatively rapid aggravation of the symptoms, above referred to, and their greater intensity early speak in favor of relapsing fever. Other signs which

may aid in establishing the differential diagnosis of relapsing fever are the absence of the eruption noted in typhoid and typhus fevers, the rather frequent occurrence of facial herpes, seldom seen in the other two typhoidal diseases, the relatively greater moisture of the skin and tongue, etc. But among all the symptoms of relapsing fever the presence of spirochætæ in the blood is the most pathognomonic. We need not here go into a description of the different appearances of the parasite, having treated of that in great detail in a previous section. In the further course of relapsing fever we find among the characteristic symptoms the rapid, critical, and extensive fall of temperature, sometimes even below the normal, at a more or less determinate period, and also the other critical phenomena which coincide with a sensible improvement in the general condition of the patient; the return of all the symptoms after the apyretic interval, and their disappearance again at the end of the relapse; the presence of spirochætæ in the blood during the paroxysms, etc. A disease having such an evolution can be confounded with no other affection whatever.

A febrile paroxysm of short duration, such as we have seen the later ones, the third and fourth, may be, and also a slight or abortive paroxysm of relapsing fever, may give occasion to confusion with malarial fever. Formerly this confusion was indeed very frequent, but at the present time, since the two diseases have been better studied, such a mistake is scarcely possible. Relapsing fever differs from intermittent fever by many important symptoms, which we have indicated above, by the greater length of the febrile paroxysms as well as of the apyretic intervals, often by the termination of the disease after the second or third paroxysm, and by its contagiousness. The most important element in the differential diagnosis of these two affections is, however, the presence of different microorganisms in the blood, of spirochætæ in relapsing fever, and of plasmodia in intermittent fever.

When there is any possibility of a confusion with other affections of whatever nature, the diagnosis can always be established with certainty if an examination of the blood reveals the presence of spirochætæ.

Another method of blood examination which may be of service in a diagnostic sense is that dependent upon peculiar properties of the serum in relapsing fever. Similar to what has been determined in regard to typhoid fever by Widal and others, Loewenthal, of Moscow, has found, starting with the experiments of Gabritchevsky, that the blood serum of a patient with relapsing fever, taken at the beginning of the apyrexial period or at the end of the febrile paroxysm, pos-

sesses bactericidal properties as regards the spirochætæ, while no such property is possessed by the blood serum of patients suffering from other diseases. These observations, however, are in need of further confirmation before the conclusions drawn from them can be accepted fully.

Formerly there was occasionally danger of confusing relapsing fever with yellow fever, as we have seen in the historical section, but at present, when the symptoms of the two affections have been so carefully studied and when we possess such a pathognomonic sign as the presence of spirochætæ in the blood, there is no danger of an error in the diagnosis. Apart from the proof furnished by an examination of the blood, the rapid and pronounced increase in size of the spleen, which does not occur in yellow fever, the periods of apyrexia and the relapses, and the low death rate will enable us to differentiate relapsing fever from yellow fever.

In certain cases complicated with jaundice, relapsing fever might be confounded with infectious icterus, called Weil's disease. Vassilieff, who has most carefully studied this latter affection, believes with good reason that in the description of bilious typhoid by Griesinger there were included many signs of various forms of jaundice and especially of Weil's disease. In such cases an examination of the blood for spirochætæ would clear up the diagnosis. We must note, however, that there are in the literature certain reports of a febrile form of icterus, supposed to be relapsing fever, which differed from the latter somewhat as regards the results of blood examination. Although in its external appearance the disease resembled relapsing fever very closely, an examination of the blood revealed certain points of difference in the microorganisms in the two diseases. Although in the cases of febrile icterus the microorganisms appeared as comma bacilli or even as bacteria twisted into spiral form, yet they differed in certain notable particulars from the ordinary spirochætæ of relapsing fever—in their appearance, in the fact of their slower movements, and in their reaction to staining agents. Karlinsky, who has observed this affection in Herzegovina, thinks that the ordinary morphological characters of the parasites and the clinical features of relapsing fever are modified by the influence of malaria; but further researches are necessary to determine with certainty whether we have to do with a modified relapsing fever or with a distinct affection.

In pseudoleukæmia we sometimes observe febrile paroxysms recurring periodically, which bear a considerable resemblance to those of relapsing fever. The differential diagnosis in these cases rests upon the same factors as in the case of the other affections which we have just been studying.

Prognosis and Mortality.

We may say in general that of all the typhoidal diseases relapsing fever is the least grave in its consequences. The death rate in relapsing fever varies greatly, according as we include or exclude in our statistics the icteric form, in which the greater number of deaths occurs. Up to within recent years most authors separated the two forms of the disease in forming their tables of mortality statistics. The death rate in bilious typhoid is high, reaching 40 per cent. in most epidemics, and sometimes even 60 per cent. or more. In the ordinary form of relapsing fever, on the other hand, the mortality is only about 3 or 4 per cent. (Griesinger, Murchison), varying from 1.8 to 6 per cent. in different epidemics, or more rarely reaching from 7 to 10 per cent., and also rarely falling below the figures above given. If we regard the two forms as one disease, which in fact they are, the mortality of relapsing fever even then will not be very large. In the municipal hospitals of St. Petersburg the death rate from relapsing fever was: in 1886, 5.9 per cent.; in 1890, 4.4 per cent.; in 1891, 6.2 per cent.; and in 1895–96, 2.6 per cent. (Likhacheff). The average mortality for the past fifteen years was 3.8 per cent.

The character of the individual epidemic on the one hand, and the hygienic conditions under which the patient lived before and during his attack on the other, have certainly a very great influence on the outcome of the disease.* The better the hygienic conditions are the better is the prognosis. In hot countries and in patients who are badly nourished or exhausted with excessive labor, the mortality of relapsing fever is higher. During the last Russo-Turkish war, in the army of the Danube, the mortality was 12.3 per cent., the total number of sick being 39,337; among the troops in Asia, however, the total number of sick being 14,576, the mortality was about 26 per cent.

The age of the patient is also an important factor, the mortality among the young and middle-aged being much less than that among those of advanced age. The following statistics from the records of the Oboukhovsky Hospital for 1877 show the influence of age on the mortality of relapsing fever: Among patients between the ages of 11 and 15 years the mortality was 1.72 per cent.; from 31 to 35 years, 7.44 per cent.; from 61 to 65 years, 60 per cent. According to Likhacheff, the mortality during the epidemic of 1895–96 at St. Peters-

* According to Zorn, during the epidemic of 1864–65, at the Oboukhovsky Hospital in St. Petersburg the mortality of the common form of relapsing fever was 16.67 per cent., of bilious typhoid 55.32 per cent., and of the two forms together 19.55 per cent. Among my hospital patients in the epidemics of 1895–96 at St. Petersburg there was not a single death in more than fifty cases.

burg was as follows: Between the ages of 16 and 20 years, 0.7 per cent.; 31 to 35 years, 2 per cent.; 41 to 45 years, 4.4 per cent.; 51 to 55 years, 13 per cent.; 66 to 70 years, 19.2 per cent.; 71 to 75 years, 45.5 per cent.

As regards sex we may say that, according to the statistics of many authors, which accord well with my own, women are more rarely attacked by the disease, but when attacked the mortality among them is slightly greater than that among men. This fact has also been noted in analyzing the statistics of several large hospitals. Douglass found exceptionally that the mortality from relapsing fever was 11.5 in men and only 5.33 in women. The relative mortality among men and women varies somewhat in the different epidemics. Thus at the Botkin Hospital at St. Petersburg, during the epidemic of 1890–91, the mortality among men was 5.1 per cent., among women, 7 per cent.; in 1885 it was 3.1 among men and 4.8 among women. Likhacheff gives the following figures concerning the mortality among the two sexes in the municipal hospitals of St. Petersburg: In 1882, men 8.7 per cent., women 12.3; in 1886, men, 4.5, women 7.3; in 1895–96, men 2.5, women 3.7 per cent. In these statistics the relatively greater age of the women may have had something to do with the greater mortality among them.

It is needless to say that certain antecedents of relapsing fever, which may have weakened the organism and left it less able to resist the onslaughts of the disease, among which we may include pregnancy, will have a malign influence on the outcome. The period at which the patient enters the hospital has also an evident influence on the prognosis, a fact which is recognized in respect to the other so-called typhoidal diseases, the earlier the patient comes under systematic treatment the better being his chances of recovery. Finally the mortality is greatly increased by the intercurrence of complications, especially nephritis, pneumonia, icterus, meningitis, infarcts and rupture of the spleen, fatty degeneration of the heart, etc. According to some recent statistics of the fatal cases of relapsing fever, published by Jogikhess, there were among men 91.43 per cent. in which some complication existed, and among women 94.12 per cent. were complicated cases, making an average for the two sexes of 91.95 per cent. of all deaths occurring in complicated cases. Of all the complications icterus, accompanied by the symptoms of the so-called bilious typhoid, and pneumonia cause the greatest number of deaths. According to the observations made at the Oboukhovsky Hospital at St. Petersburg during the epidemic of 1877, the mortality due to the complication with jaundice was in men 34.28 per cent., and in women 17.65 per cent. According to the report of the Botkin Hospital at

St. Petersburg for the five years from 1882–86, the mortality of bilious typhoid (regarded at that time as a distinct morbid entity) was 56.2 per cent., while for all other non-complicated cases of relapsing fever it was only 3.4 per cent. Ponfick found among the deaths from relapsing fever 60 per cent. due to the complication with pneumonia, 20 per cent. due to complications on the part of the spleen (rupture, abscess, secondary peritonitis or pleurisy, etc.), and 8 per cent. due to fatty degeneration of the heart.

Death in relapsing fever may occur during the period of apyrexia or in the febrile paroxysm as a direct consequence of the intensity of the infection. The weakening of the heart, the excessive temperature, symptoms of collapse and those indicating cerebral implication, profuse diarrhœa, and extreme general debility consequent upon profound intoxication are all very grave symptoms from a prognostic point of view, since they point in relapsing fever, as well as in the other typhoidal affections, to an approaching fatal issue.

It will be interesting to see how the prognosis varies according to the different periods of fever and apyrexia, and it will be no less so to learn whether we can foresee the occurrence of relapses by a careful study of the symptoms at any given time. As regards the first of these points, there is a belief, based upon observations made during the early epidemics, that most of those who die from relapsing fever do so in the second febrile paroxysm, or first relapse, though many also die at the height of the primary attack (Griesinger). More recent observations strengthen this belief, but show us that there is a slight preponderance of deaths during the primary paroxysm. We see this, for example, in a study of the statistics of the Botkin Hospital at St. Petersburg. In the epidemic of 1890–91, 50.48 per cent. of those who died from relapsing fever had but one febrile paroxysm, 39.8 per cent. had two, 7.76 per cent. had three, and 1.94 per cent. had four distinct paroxysms of fever. All those who had five or six paroxysms recovered eventually. We see from these figures that the greater number of deaths occurs in the first two febrile paroxysms, and especially in the first. If, however, we take into consideration the fact that the number of those who have many relapses is rather restricted, we shall readily see that the statistics above cited do not express very exactly the degree of danger associated with the third and subsequent paroxysms. Still if we divide the cases according to the number of attacks, and then count the number of fatal cases in each of these categories, we shall obtain a confirmation of the statements made above. If, for example, we analyze in this fashion the statistics above cited concerning the epidemic of 1890–91, we find that the total number of patients who had but one paroxysm was 633,

and of these 52, or 8.2 per cent., died. The number of patients who had two attacks (one relapse) was 699, and of this number 41, or 5.8 per cent., died. Of those who had three febrile paroxysms there were 379 with 8 deaths, or 2.1 per cent. There were 47 who had four attacks, and of these 2, or 4.2 per cent., died. Among the 10 patients who had five paroxysms of fever and the 2 who had six, there were no deaths. We see, therefore, that the greatest danger exists during the first two febrile paroxysms, and that this danger diminishes in the third and fourth paroxysms, the third being apparently slightly more favorable than the fourth, although the statistics are not full enough to enable us to come to any positive conclusions as between the two in this respect. In regard to the periods of apyrexia also we have too few data to enable us to affirm anything with certainty. It is most probable that each apyrexial period being united to the preceding febrile paroxysm, shares with the latter its peculiarities as regards prognosis. According to the statistics of the Oboukhovsky Hospital at St. Petersburg for the year 1887 (1,288 patients), it would appear that death occurs most frequently during the second period of apyrexia, and this corresponds also with the opinion of Meschede.

As regards the total duration of the disease and the length of hospital stay required, we may cite the following statistics: According to the observations of Müllendorf, made in Dresden in 1879, in cured cases about forty days elapse before the patient is fully restored to his normal strength and weight. The hospital stay averages thirty days. In the Russian hospitals the time spent in hospital is somewhat different. In the Botkin Hospital at St. Petersburg during the epidemic of 1882–83 the average stay of those who died was 31.5 days, of those who recovered was 31.2 days. During the epidemic of 1885–86 the average stay of those who died was 27.5, of those who recovered it was 23, and of all patients taken together it was 23.4. During the epidemic of 1890–91 the figures were, for the recovered 25.9 days, for the dead 14.9 days, and for all together 25.2 days. According to Jogikhess the total duration of the disease from its invasion to the day of death is for men 20.159 days, for women 25.562, and for both together 21.253; in the cases ending in recovery the average duration of the disease is for men 25,603, for women 25.223, and for both together 25.540 days. As regards age the shortest duration of relapsing fever is in patients between the ages of 11 and 15 years (22.759 days) for males, and between the ages of 26 and 30 years (18.039 days) for females.

An attempt has been made to foretell the occurrence of subsequent paroxysms in those who have already had one. Many and varied researches have been made in this direction, but have not yet given

any satisfactory results. The various clinical phenomena characteristic of the disease are of very slight utility in enabling us to determine whether or not another febrile paroxysm will occur. Motchoutkovsky had remarked that the course of the temperature in the apyretic period varies, and he believes that careful thermometric observations made at this period will furnish an indication as to whether or not another paroxysm will take place. His rule is that if, after the crisis and a considerable fall of temperature (below normal), the temperature begins to rise rapidly and progressively by some tenths of a degree Centigrade each day and presents well-marked oscillations in the course of the twenty-four hours (1.5° up to even 2.5° C. = 2.7° to 4.5° F.) so that by the fourth day it has reached 37.8° C. (100° F.), then we may expect a relapse to take place. If, during the period of apyrexia, the temperature mounts very slowly and to a slight extent, or if, after the critical fall, it rises rapidly a degree and a half Centigrade, and then remains at this level, the recurrence of fever is less probable and may be looked for in not more than sixty per cent. of the cases. The prognosis is still less certain if the temperature curve shows marked oscillations (one degree) from the first day, or weaker ones (half a degree), the average remaining at about the same level from day to day. Such a curve, however, would rather tend to show that the patient is threatened by a new attack of fever. Although these rules are by no means without their exceptions, they are nevertheless applicable to a large number of cases. Unfortunately the complications, even the least serious ones, as bronchitis for example, or other unimportant factors, such as sweating, may influence the course of the temperature during the apyretic period and so vitiate the prognosis. Oks says, however, that he has confirmed the value of the first-mentioned rule in twenty-two out of twenty-four cases. Motchoutkovsky has called attention to another type of temperature curve which is of value in a prognostic sense, as implying a probable freedom from relapse. This is when the temperature continues to descend gradually during the four days succeeding the crisis. The prognosis in such a case is more definite than in those just mentioned, and we can exclude with considerable certainty the occurrence of any relapse. Oks found the rule to work in ten cases out of twelve.

Senetz believed he could foretell whether a relapse would or would not occur according to the amount of solid constituents in the urine during the period of apyrexia. But we have already seen above that the quantity of urine excreted and its specific gravity vary within wide limits during the course of relapsing fever, and although the increase and decrease in this excretion bear a relation to the tempera-

ture, we can hardly base any prognosis as to relapses upon such variations.

Gabritchevsky has noted the presence of bactericidal properties in the blood of patients with relapsing fever who have passed through a febrile paroxysm, and recently Loewenthal of Moscow has utilized this fact in order to establish a method of prognosis as to the occurrence of relapses. As a result of his researches he concludes that a relapse will not occur if, on the seventh day of the apyrexia, the bactericidal reaction is produced within less than an hour.

Prophylaxis.

Relapsing fever is almost as contagious a malady as is typhus fever. It attacks especially the members of the poorer classes of society and those who live under bad hygienic conditions, and after these, physicians, hospital attendants and nurses, clergymen, etc.—in a word all those who by their occupations are brought into close relations with the poor. This furnishes us with clear indications as to what measures ought to be taken in order to prevent the spread of infection. It is not in the power of science always to prevent the importation of the contagion. But we can without doubt do much, after the disease has declared itself, to localize it and limit the epidemic by means of appropriate sanitary measures. In the first place we must clean up all the rookeries which are filled with an unwashed and filthy crowd of tenants, among whom the contagious principle finds a favorable soil for its growth and extension. We should reduce the crowding, purify the air, see that the water supply is pure, and pay attention to the quality of the food. We must especially look to the centres of contagion, night refuges, prisons, etc. It is indispensably necessary to cleanse and disinfect not only the lodgings of the sick, but also all utensils, furniture, and clothing which may serve as vehicles of contagion, and particularly beds and other things which harbor the insects that may transport the spirochætæ of relapsing fever from the sick to the well.

In order to limit the epidemic it is very necessary, as in the case of other diseases of this class, to take note of the first cases; and where relapsing fever is prone to occur, a domiciliary inspection, such as is made in case of a cholera epidemic, for example, may be of the greatest service. Finally we must isolate the sick as early as possible, removing them to hospitals and disinfecting the premises whence they were taken. The clothing of the sick should also be thoroughly disinfected, and objects of small value which cannot be properly disinfected, as straw bedding for example, should be burned.

In hospitals the patients should be isolated, but it is unnecessary to carry this to extremes, and it is even not absolutely necessary to place all the patients with relapsing fever in a ward by themselves, provided the ward is large and well ventilated and the beds are not placed too close together. I have never seen a case of contagion occurring in a hospital ward where precautions of the nature just mentioned were observed. During summer epidemics treatment in tents or in large and open barracks is preferable to that in hospital.

As regards personal prophylaxis some experiments have been made in recent years with a view to produce immunity by means of the serum of one who has just passed through an attack of the disease. We have seen that the serum of such a one does possess more or less bactericidal properties, and the fact that succeeding paroxysms tend to become shorter and shorter and finally to remain away altogether points to the acquisition of at least a temporary immunity. Metchnikoff contends that this immunity is due to phagocytosis, and so it may be in a measure, but the researches of Buchner, Pfeiffer, and others have shown us that blood serum free from all cells, and also the serum of other animals than man, may be endowed with bactericidal properties as regards certain microorganisms. We have already mentioned the experiments of Ivanoff in producing artificial immunity in monkeys by the injection of blood serum removed from a person who had had several paroxysms of relapsing fever. The monkeys which received no serum injections suffered from characteristic attacks of relapsing fever, while those which had been previously treated escaped with a slight febrile reaction, and no spirochætæ could be found in their blood.

Treatment.

Gabritchevsky claims to have obtained good results in forty cases of relapsing fever in man treated by injections of serum from animals which had been immunized by repeated injections of blood containing Obermeier's spirochætæ. The injections were made during the first period of apyrexia and resulted in fifty per cent. of the cases in preventing any relapse. Loewenthal also treated patients suffering from relapsing fever with injections of serum taken from other patients during the period of apyrexia. Thirty-nine out of 84 patients so treated (46.43 per cent.) during the first apyrexial period had no relapse, while out of 152 patients who had no specific treatment only 25 (16.45 per cent.) escaped a relapse. These results, as well as those related in the section on etiology in respect to animal experiments, although far from being absolute, are nevertheless of undoubted importance, and are sufficiently encouraging to justify us

in hoping for definite success in the near future. Unfortunately it is impossible, for the present at least, to study this question after the methods employed in the case of some other of the contagious diseases (attenuation of the specific microbes or their products), since we are unable to obtain cultures of Obermeier's spirochætæ.

Starting from the experimental facts above mentioned of the influence of certain substances upon spirochætæ outside of the animal organism, many have endeavored to treat the disease by means of the administration of such of these substances as had been found to be the most injurious to the specific microorganism. Other remedies which were known to exert a more or less restrictive influence upon cyclic or periodic processes have also been tried. Among the substances belonging to these two categories the following have been employed: quinine, strychnine, arsenic, salicylic acid, potassium iodide, potassium permanganate, creosote, chlorinated water, and sodium chloride (given internally in very large doses). The results obtained, however, have not justified the hopes based upon experiments outside of the body. This can readily be understood when we reflect that it is impossible to introduce into the body, without injury to it, any of these substances in sufficient quantity to destroy the specific organisms. Furthermore, we cannot be certain that the same effect will be exerted by a substance introduced into the living organism as we see caused by it in test-tube experiments.

Theoretical conclusions aside, however, we find that some drugs do exert a beneficial influence on the course of the disease whatever may be the correct explanation of their action. Among these substances quinine occupies the first place. We have seen above that the hydrochlorate of quinine, even in 0.1-per-cent. solution, exerts a markedly paralyzing influence upon the spirochætæ, arresting their movements completely. We can of course never obtain such a concentration in the blood of the living, but nevertheless clinical experience has shown that the drug in ordinary doses of 0.6 to 2.0 gm. (gr. ix.–xxx.) a day, given in solution by the mouth or rectum, acts better than any other remedy in grave forms of relapsing fever, especially in bilious typhoid. According to Griesinger, the effect of this drug in bilious typhoid is as marked and as certain as it is in malarial fever. Nevertheless he was unable to cut short an attack at its beginning by means of quinine, and few other clinicians have obtained any specially good results with the administration of quinine in relapsing fever.

Among the other agents which are known to influence the life and activity of pathogenic microbes, and which have found an application at the bedside, we have to mention the mercurials. In 1881 Oks em-

ployed calomel (calomel and white sugar, each 0.25 gm. = gr. iv., every three hours) in the treatment of relapsing fever, and claimed that in sixty per cent. of all his cases so treated there were no relapses, the disease consequently being limited to one paroxysm. Under other methods of treatment more than one febrile paroxysm occurred in all but twenty per cent. Oks found also that in cases in which a relapse occurred in spite of the administration of calomel, the duration of the first apyrexial period was prolonged by more than two days on the average. Oks does not attribute any special effect to the slightly purgative action of the calomel, since no such results are obtained by the administration of other cathartics, but believes that the drug is a specific remedy for relapsing fever. He himself admits, however, that his observations are not entirely convincing, since in addition to the administration of calomel he had also recourse to cold packing. We may add also that the results claimed by Oks have not as yet been confirmed by other observers.

Certain authors are inclined to regard both arsenic and methylene blue as specifics in the treatment of relapsing fever. Bogomoloff reports four cases in which very favorable results were obtained by the internal or subcutaneous administration of Fowler's solution, and he thinks the remedy may even cut short an attack of the disease. Others, however, have not been able to verify the experiences of this author. Nikolsky did, indeed, obtain good results from the administration of arsenic in relapsing fever, but only as regards relief of the cephalalgia and muscular pains.

Afanassieff and Seyliger regarded methylene blue as possessed of specific virtues in relapsing fever, but they did not find that it shortened the febrile paroxysm more than one full day in the fifteen cases in which they tried it (in the rather large dose of 0.3 to 0.4 gm. not less than three times a day) from the very beginning of the attack. On the other hand the use of this remedy has not only not given good results in the hands of other clinicians, but it has even produced rather unpleasant side effects, such as albuminuria, vomiting, etc.

Potassium iodide is another remedy which has been tried more or less perseveringly in the treatment of the disease under consideration. The experiments above mentioned in the section on etiology (page 473) have shown that this drug exerts a quite marked influence upon the spirochætæ outside of the body, and it was for this reason that I made use of it in my clinic during the epidemic of 1895–96. At the beginning it seemed to prevent a relapse in several of the cases in which it was exhibited, but a continued use of the remedy in other cases showed that it was really without influence in this respect, patients who were taking it being as subject to relapses as those to

whom it was not given. I ought to say, however, that the drug was given in quite moderate doses in all these cases, not exceeding 0.3 gm. (gr. v.) three or four, rarely six times a day, and I think it is certainly deserving of further trial in larger doses.

To what we have just said concerning the various therapeutic measures employed at various times and by various clinicians in the treatment of relapsing fever, it will be proper to add a few words in regard to Motchoutkovsky's method. As we have seen above, this author regarded the inspissation of the blood as the cause of the death of the spirochætæ and the termination of the febrile paroxysm, basing his belief upon the great loss of fluids occurring at the crisis and upon the deleterious effect upon the microorganisms (outside the body, be it said) of certain hygroscopic substances, such as glycerin and sugar. He therefore endeavored to arrest the progress of the disease by forced sudation, induced by the wet pack and the internal administration of jaborandi, combined with the restricted ingestion of fluids. He asserted that the number of spirochætæ in the blood diminished one-half when sweating was induced by the wet pack, and disappeared entirely under the influence of jaborandi. The duration of the febrile paroxysm was also shortened. He believed that the use of purgatives might produce an equally beneficial effect, and in this was in accord with Griesinger who had made the same observation long before him. But we have seen above that the blood in cases of relapsing fever does not become inspissated to any great degree, but that on the contrary its specific gravity usually diminishes during a febrile paroxysm in this disease; and Oks furthermore failed to obtain any effects from the use of purgatives, with the exception of calomel, the latter, moreover, being administered in only feebly laxative doses. Finally no other clinician has been able to confirm the results claimed by Motchoutkovsky.

In reviewing what we have just discussed concerning the employment of medicaments and methods regarded by their proposers as specific in the treatment of relapsing fever, we are forced to conclude that not one of them possesses the power of cutting short an attack of the disease or of preventing a relapse.

Since, therefore, we have as yet no specific method of treatment of relapsing fever, we find ourselves reduced to a purely expectant and symptomatic treatment, placing the patient under the most favorable hygienic conditions, and making use of the ordinary therapeutic measures that are employed in the case of the other typhoidal diseases—typhus and typhoid fevers. The hygiene of the patient is a very important factor in the successful management of the disease. Cleanliness, rest in bed in a large and well-aired room with a moder-

ately low temperature (14° or 15° C.—57° to 59° F.), and a suitable diet are the essential conditions of successful treatment.

The *diet* should be light and at the same time substantial. We may give beef-tea with an egg, chicken broth, a little veal or tender beef, not too fat, beef juice, milk, and wine. If the patient has a good appetite we may sometimes give him some of the more digestible vegetables, beef or chicken-hash, or the like, but as a general rule a liquid diet should be adhered to. In addition to furnishing the most perfect food for the human organism, milk is also of great service in the way of elimination of the toxins which poison the organism in this and other similar infections. The quantity of milk taken at any one time should be limited, one-quarter to one-half a glass every hour or oftener, about two quarts being ingested in the course of the twenty-four hours. Some patients exhibit a repugnance to milk, especially when it is given after being boiled. In such cases it may be taken raw, or its taste may be disguised by mixing it with a little coffee, cherry brandy, or the like. We may also substitute kephir, which is often tolerated when plain milk is rejected, and which may also be useful by reason of the alcohol and lactic acid which it contains. In order to quench the thirst which is sometimes very distressing we may give pure water, boiled if there is any suspicion as to its quality, weak tea, acidulated drinks made from vegetable acids, such as lemonade without too much sweetening, or from dilute mineral acids, such as hydrochloric acid (4 to 8 parts in 720) or phosphoric acid (8 to 15 parts in 720). These mineral acids tend to correct the diarrhœa from which many of these patients suffer, and at the same time promote antisepsis of the digestive tract. A potion containing a somewhat larger proportion of hydrochloric acid (tablespoonful doses every two hours of a mixture of dilute hydrochloric acid 2 parts, raspberry syrup 15 to 30 parts, and distilled water 130 to 150 parts) may be prescribed in mild uncomplicated cases for the moral effect—*aliquid faciendum.*

Among the symptoms of relapsing fever which may inspire more or less fear in the physician, and in any case will especially attract his attention, is the elevation of temperature. It is ordinarily higher in this disease than in either typhus or typhoid fever, reaching often 41° to 42° C. (105.8° to 107.6° F.) or even more. Ought we to attempt to reduce this high temperature in relapsing fever, and if so how must we proceed? There is great diversity of opinion on this point among the different authorities. While some, as Liebermeister, Jürgensen, and to a certain degree Ziemssen, regard the fever as an element injurious to the organism, others look upon it as possessing in itself a curative property. The relatively short duration of the febrile parox-

ysms in relapsing fever and also the very high temperature lend to the fever in this disease a peculiarity all its own, and for this reason the arguments based upon experience in other pyretic affections are not wholly applicable to this. Indeed, we know that relapsing fever is the very disease which of all others has led medical thinkers to look upon the febrile process as one influencing favorably the course of an infectious disease. It has been claimed that the high temperature is the factor which puts an end to the disease, this belief being based upon the fact to which we have referred above (page 471) that temperatures of 40.5° to 41° C. (104.9° to 105.8° F.) exercise a very marked influence upon the movements, that is to say the life, of the spirochætæ. Heidenreich admitted that the termination of the febrile paroxysm in relapsing fever is justly attributable to the high temperature occurring before the crisis. It has been found that still higher temperatures exert a still more paralyzing influence upon the micro-organisms, but such temperatures also influence unfavorably the cellular elements of the human organism, giving rise to functional troubles or even very pronounced anatomical changes in the vital organs. On the other hand recent investigations have shown us that there are other factors even more injurious to the life of the spirochætæ than is an elevated temperature; these are the phagocytes, antitoxins, bactericidal substances, etc. Perhaps a certain elevation of temperature is favorable to the elaboration of these substances or to the phagocytic action of the leucocytes. But no one, so far as the writer knows, has ever noted any such effect or has demonstrated it convincingly. Certain authors have, it is true, noted the fact that very high temperatures favor in general granulofatty degeneration of the cellular elements, and at the same time they may be favorable to the destruction of the leucocytes at the expense of which the bactericidal substances are elaborated. But this action of high temperatures cannot of course pass a certain limit without becoming most injurious to the organism, and for this reason the therapeutist must without doubt seek in certain cases to limit the rise of the temperature of the body. The unfavorable action of high temperatures upon the human organism is too well known to call for discussion here, and we need only remark that an elevation of the temperature considerably above the normal exerts a peculiar toxic action upon the muscular tissues, not only of the striated skeletal muscles but also of that of the heart. An excessive temperature also exerts an injurious influence upon the parenchymatous and glandular organs, but especially upon the nervous system, beginning with the respiratory centres. This action of unduly elevated temperatures is exerted without doubt in relapsing fever as well as in other pyrexial diseases, since a very long continuance of

high fever is not at all necessary in order that injury may be done to the histological elements of the organs of the body. My experiments upon rabbits have shown that, if their body temperature is raised some 4° or 5° C. (7.2° to 9° F.) above the normal (a not at all uncommon occurrence in relapsing fever in man), an injurious effect will become manifest in four or five hours when the pyrexia has been repeated two or three times and occasionally when it has occurred but once. I would also draw attention to the demonstrated fact that one effect of a very high temperature is to paralyze the regulatory heat centres. We see this sometimes in the case of animals which have been exposed to very high temperatures; after they have been removed from the hot chamber their temperature not only does not fall but even continues to rise above that which they had while they were exposed to the heat. The same fact has often been observed in man after exposure to similar conditions. Hyperpyrexia (from 4° to 5° C. = 7.2° to 9° F. above the normal) should therefore be looked upon as dangerous to life and as offering an urgent indication for therapeutic interference. And even if we believe that high temperatures are prejudicial to the existence of the spirochætæ, we yet cannot give them free rein and allow the fever to rise to an extreme height. A moderate elevation of temperature (2° or 3° C. = 3.6° to 5.4° F. above the normal) in relapsing fever, other conditions being favorable, need cause no apprehension on the part of the physician and calls for no therapeutical interference.

What are the remedial measures to which we must resort in cases in which the hyperpyrexia calls for medical intervention? We are in possession at the present time of very many agents of undoubted power in this direction, and there is no difficulty in lowering at will the temperature of a patient to a certain degree. We have a whole series of internal antipyretics from which to choose when we wish to obtain this effect, and their number increases daily. We may also lower the body temperature by means of refrigeration externally applied. It is very evident that the effects of externally applied refrigeration will differ essentially from those produced by the administration of antipyretic drugs internally; the mode of action in the two cases is also essentially different. The internal antipyretics lower the temperature chiefly by causing a loss of heat in consequence of hyperæmia of the skin and increased perspiration. At the same time most of these substances, with the exception of the salicylates, the benzoates, and cresotinic acid, also retard the metabolic processes and diminish the excretion of carbonic oxide and of urea. Very different are the results obtained by external refrigeration. Limiting our observations to the most effective of these methods, namely, the cold bath, we see

that its influence on the skin is manifested especially by contraction of the cutaneous vessels and diminution of the secretions of the skin. Thanks to this there is an afflux of blood to the internal organs resulting in the establishment of an increased excretion of urine, an augmented calorification, a more pronounced absorption of oxygen, increased metabolism and heightened excretion of its products (carbonic oxide and, according to certain authors, urea), and also an excretion of toxins. All these effects are very favorable to a happy issue of the morbid process, but they cannot be obtained by the internal administration of antipyretics whose action is so different or even diametrically opposed to this. Furthermore, these internal antipyretics exert a chemical action, which is far from being wholly indifferent, and may indeed produce some most undesirable side effects, such for example as that of antifebrin on the blood, etc.

In coming to a determination, in any given case, as to the method of refrigeration to be employed, we must remember that the effects above mentioned of the internal antipyretics may be very undesirable in a disease such as relapsing fever. In this affection sweating, even during the course of the febrile paroxysm, is by no means a rare phenomenon; and furthermore, after the crisis the temperature often falls to a very undesirable depth, and this fall is accompanied by symptoms of collapse, which may lead to a fatal issue. These considerations will therefore lead us to conclude that the method of external refrigeration is the preferable one, since it is the most powerful, the most easily controlled, and the best adapted to stimulate the oxidizing processes in the body. While exercising a marked influence upon the circulation, changing its course and distribution in the body, this may also modify in a favorable sense the anatomical processes in the organism. So far from introducing harmful substances into the body this method of treatment contributes, on the contrary, to the elimination through the kidneys of injurious products circulating in the blood, and also to the increased excretion through the lungs of carbonic oxide. We need not speak of the value of baths from the point of view of cleanliness, although this is sometimes a matter of considerable importance in the case of a not inconsiderable proportion of the patients suffering from relapsing fever who are brought to hospital.

What we have just said does not exclude, however, the employment of internal antipyretic remedies in relapsing fever. On the contrary, there are certain cases in which their use is indicated. We should select by preference those of this class which are not only antipyretic but also bactericidal, and those whose advantages, when given in a certain way and in special cases, will outweigh their dis-

advantages. The number of internal antipyretics is very great and it is impossible to judge of them all *en bloc*. In proof of this we need only recall the difference as regards their effects upon metabolism between quinine and salicylate of sodium, the former diminishing the excretion of carbonic oxide and of urea, the latter increasing the excretion of urea, but exerting no influence upon that of carbonic oxide. The use of certain internal antipyretics in combination with cold baths may find a rational application in the treatment of grave forms of relapsing fever. Among the remedies of this class which have recently found some favor are lactophenin and phenacetin in moderate doses of from 0.3 to 0.5 gm. (gr. v. to viij.) two or three times a day. An indication for the employment of these remedies may also occasionally be found in the presence of cephalalgia and muscular pains.

The methods of application of external refrigeration are extremely variable. In cases of ordinary severity the graduated bath is especially to be recommended, beginning with a temperature of 35° C. (95° F.) and reducing to 30° or 29° C. (86° or 84.2° F.). Equally serviceable are tepid baths of a temperature of 35° to 32° C. (95° to 89.6° F.) of fifteen to twenty minutes' duration, the effect of which is similar to that of the graduated bath, though slightly less pronounced. If the temperature is very high and the action of the heart is yet sufficiently strong, more energetic refrigeration may be indicated, such as cool baths of 25° to 19° C. (77° to 66° F.) for ten or twelve minutes; but if the heart is weak and there is marked general exhaustion, we may use the cold wet pack.

In cases in which the temperature is very high, yet the disease otherwise does not appear to be of great severity, we may employ the tepid baths above mentioned, gradually cooled from 35° down to 31° C. (95° to 87.8° F.) by the addition of cold water. By this method we avoid the unpleasant sensations caused by cold baths and at the same time are able to reduce the temperature and to moderate the disagreeable symptoms accompanying high fever.

While employing these baths, we may also give small doses of antipyretic remedies internally (for example, lactophenin, in doses of 0.3 gm. = gr. v. three times a day, or quinine 0.2 gm. = gr. iij. three or four times a day). No unpleasant symptoms are caused by these small doses, the temperature remains at a moderate elevation, and convalescence is normally established. In addition to the treatment above outlined, I habitually order wine, Madeira or port, two or three glasses a day, taken in small quantities, especially after the bath.

Such is the treatment employed in my clinic, and which has given me extremely favorable results, as shown by the fact that for the last

three years I have had no death to deplore among my patients, nor have any of them suffered from severe complications.

On account of the possible occurrence of heart failure the attention of the physician must always be directed to the condition of this organ. Weakness of the heart, as shown by a very rapid and weak pulse and especially by irregularity, is a frequent symptom in relapsing fever, and one offering an urgent indication for stimulants and cardiac tonics. One of the best heart tonics for use in these cases is wine. Among the strictly medicinal remedies may be mentioned camphor, which is of value especially during the febrile paroxysms. It may be given in the form of powder, one or two grains at a dose several times a day, or in emulsion in similar doses; it is better, however, to give it in the form of powder mixed with two or three grains of quinine. Each powder may be taken in a little wine, or may be followed by it. If we find it necessary to obtain a more energetic and rapid effect we may resort to subcutaneous injection of camphorated oil (1:10), a syringeful corresponding to about a grain and a half of camphor. This injection may be repeated several times a day if the patient's condition calls for it. In cases in which a very rapid stimulation of the heart is needed we may resort to subcutaneous injections of ether, which is perhaps more rapid in its action than camphor, but, on the other hand, not so permanent. In addition to its tonic effect, camphor undoubtedly possesses the power of regulating the heart's action in cases of arrhythmia. We must not forget also that camphor is endowed with antipyretic properties, very slight it is true, which may be of service in cases of high fever. It is at the same time a stimulant of certain other cerebral and medullary centres (respiratory centres, etc.). All these contribute to render camphor one of the most valuable and certain stimulants for use in cases of relapsing fever with high temperature and weak heart.

The preparations of musk and valerian, especially the ethereal tincture, strong coffee or caffeine, and other similar remedies are also indicated as stimulants, tonics, and regulators of the heart's action. I have personally several times had occasion to convince myself of the excellent stimulant effect upon the heart of tincture of musk, having employed it especially in the algid stage of Asiatic cholera. In patients whose pulse was wholly imperceptible the administration of tincture of musk was followed by the reappearance of the pulse. In half an hour or an hour later the pulse might again become imperceptible, but another injection would excite the heart to fresh and stronger contractions, and it would again become possible to count its pulsation. In this way I have been able to maintain the action of the heart during the critical period, and so save the patient's life.

In cases of depressed cerebral action, unconsciousness, stupor, etc., we employ the same stimulants as in cases of heart weakness, namely, camphor, valerian, wine, etc. In cases of delirium in alcoholic subjects chloral hydrate, bromide of potassium, or morphine is especially indicated. If the delirium is associated with very high fever we may obtain benefit by an ice bag or cold compresses to the head. The application of cold also gives excellent service in cases of severe headache during the febrile paroxysm. In the latter case also much benefit may be derived from the use of phenacetin, lactophenin (0.3 gm. = gr. v.) or even antipyrin (0.6 gm. = gr. x.), lactophenin being rather the favorite. These same antipyretic and analgesic remedies may render good service in the relief of the osseous and muscular pains. These pains may also be greatly mitigated by means of frictions with chloroform liniment or the like. If the pains are localized we may apply warm compresses, and if they are very severe we may be obliged to resort to hypodermic injections of morphine. When the pain in the spleen is very severe an ice bag applied to the left hypochondrium may be of service, and the same may prevent rupture of the spleen from excessive hypertrophy. The same effect in these cases may sometimes be obtained by means of hot applications.

The intestinal troubles when present may often be relieved by hot applications. When the diarrhœa is very obstinate we may have recourse to the internal administration of salicylate or subnitrate of bismuth, tannin, tannalbin, salol, opium, etc., either singly or in combination. For the relief of constipation we may resort to enemata or to the internal administration of mild laxatives. At the beginning of the disease we ordinarily give a dose of castor oil or of calomel, often beginning with a dose of gr. v.– x. (0.3 to 0.6 gm.) of calomel, followed a few hours later by a dose of castor oil.

For the relief of vomiting, which is often quite troublesome in cases of relapsing fever, we may give opium or codeine with bismuth, ice pellets, or sweet almond emulsion, taken alone or in combination with opium or mild stimulants. Hydrochloric-acid lemonade, chloroform water, or oxygen inhalations may also be employed in these cases with good results.

When epistaxis becomes menacing by either its duration or its intensity, we may obtain good results by the application of a solution of hydrochlorate of cocaine (1:10) or of antipyrin (1:5). In more obstinate cases we may be obliged to resort to plugging of the nostrils and then the tampon may be moistened with one of the above-mentioned solutions.

Pneumonia, which is not a very rare complication in relapsing fever, should be treated according to the indications by counter-irri-

tation, stimulants, and expectorants. The other complications are also to be treated *secundum artem*. Abscesses, especially those of the parotid gland, should be opened as soon as possible. Morphine for the pain and local blood-letting are indicated in otitis media or interna in case suppuration has not yet occurred. Very good results also may be obtained by instillation of a few drops of carbolated glycerin (five per cent.) into the external meatus. When pus is already formed it must be evacuated by puncture of the drum membrane, and antisepsis must then be practised by syringing with a solution of carbolic acid (one per cent.) or of boric acid (two per cent.), or boric acid in powder may be insufflated into the ear.

During convalescence patients whose strength is greatly reduced should receive a strengthening diet with wine and tincture or decoction of cinchona, together with pepsin, hydrochloric acid, or some iron preparation, such as the lactate or the albuminate. In such cases Blaud's pills often render excellent service. Some of the more recently introduced preparations of iron, such as hemol, hemogallol, ferratin, etc., have been used with much success, but so far as my own observations and those of Dr. Müller in my clinic enable me to judge, these new remedies are not ordinarily so useful as Blaud's pills.

We should keep in the hospital for a time those patients who have had relapsing fever and who may be threatened with a relapse, even though they may regard themselves as well and able to resume their former occupation. These patients should be enabled to regain their strength before returning to the places where they contracted the disease, otherwise they are exposed to relapses or to a reinfection. Furthermore, while their condition remains weak as a result of the attack of relapsing fever they are peculiarly disposed to contract any other contagious disease, to the infection of which they may accidentally be exposed.

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TYPHOID FEVER.

(ETIOLOGY AND GENERAL PATHOLOGY.)

BY

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TYPHOID FEVER.

(ETIOLOGY AND GENERAL PATHOLOGY.)

Definition.—Typhoid fever is a state of infection by the typhoid bacillus. A profound intoxication is commonly produced as well as certain anatomical lesions.

Synonyms.—The following names, applied to this disease at different times and in different parts of the world, are taken from Murchison's list: Typhus nervosus (Sauvages, 1760), abdominal typhus, Unterleibstyphus (Autenrieth, 1822), fièvre typhoïde (Louis, 1829), typhus entericus (Ebel, 1836), typhoid fever (Stewart, 1840), ileo-typhus (Griesinger, 1857), endemic fever, autumnal fever (Flint, 1852), pyretus hemitritæus (?) (Hippocrates), febris semitertiana (?) (Galen), remittent fever (Sutton, 1806), febris lenta (Forestus, 1591), slow fever (Strother, 1729), common continued fever (Armstrong, 1816), nervous fever (Gilchrist, 1734), slow nervous fever (Huxham, 1739), Nervenfieber, fièvre nerveuse, low fever, febris putrida (Riverius, 1623), fièvre ataxique (Pinel, 1798), sepimia (Hare, 1853), miliary fever (Pringle and De Haen, 1760), febris gastrica (Ballonius, 1640), fièvre méningo-gastrique (Pinel, 1798), epidemic gastric fever (Cheyne, 1833), febris biliosa (?) (Galen), bilious fever (Pringle, 1750), biliogastric fever (Copland, 1844), bilious continued fever, febris mesenterica maligna (Baglivi, 1696), febris intestinalis vel mesenterica (Riedel, 1748), fièvre entéro-mésentérique (Petit and Serres, 1813), enteritic fever (Mills, 1813), entero-mesenteric fever (Abercrombie, 1820), febris mesaraica (Wendt, 1822), dothinentérite, or dothinentérie, corrected later to dothienentérite (Bretonneau, 1826), fever with affection of the abdomen (Allison, 1827), fever with ulceration of intestines (Bright, 1829), gastroenteric and gastrosplenic fever (Craigie, 1837), enteric fever (Ritchie, 1846), intestinal fever (W. Budd, 1856), night-soil fever (Brown, 1855), cesspool fever, pythogenic fever (Murchison, 1858). In this country the term typhoid fever is more commonly used than any other, though "enteric fever" is preferred by some, and we often read "autumnal fever" in the writings of the early and middle part of this century.

The Greek word τῦφος means smoke, vapor, and hence a cloudi-

ness of mind, folly, or stupor arising from fever, and we find it used by Hippocrates as a name for various affections in which the mind was clouded. During the eighteenth century and the first part of this century the name typhus was applied to the two diseases which we now distinguish as typhus and typhoid and to cases resembling them. The name typhoid was proposed by Louis, who wrote in 1829: "I have long searched for a word to express the anatomical character of this disease which would not be disagreeable to the ear, and having failed to find such an one I have adopted the expression 'affection typhoïde' as being at least free from inconveniences."

History.

It is likely that typhoid fever has prevailed among men from prehistoric times. Certain cases related by Hippocrates, although his clinical histories are hardly such that we can base any confident diagnosis upon them, still lead us to believe that among the many fevers which he observed some were typhoid. In writing of the epidemics of the fifth century before Christ, the century of Pericles, he describes a group of cases which occurred in the course of the summer and autumn with moderate disorder of the bowels, not much cough, not generally intermitting, sometimes with a crisis, which occurred most frequently by the fortieth day, but often ending in an irregular manner without any crisis and usually followed by relapse. He writes again of quotidian, internal, and wandering fevers occurring during the autumn; some of the victims continued to keep about, while others were confined to bed, with no intermissions, but having exacerbations in the tertian form. We can hardly agree with Wunderlich when he pronounces every case related by Hippocrates in the first and third books of the Epidemics to be typhoid fever. Galen's hemitritæus or febris semitertiana, or at least a portion of the cases to which he gave those names, is thought to have been in reality typhoid, and there is little doubt that the "hemitritæus" of later writers was really this disease. The description given by Spigelius of the fever which went by this name and was common in various parts of Italy early in the seventeenth century leaves little doubt of the identity of the disease. He mentions as symptoms abdominal pain, urgent diarrhœa, bloody stools, stupor, delirium, irregular remissions, and absence of marked crises, and, in some cases, relapses. He reports several autopsies which showed inflammation, some of them gangrene, of the small and large intestine. Spigelius, writing "de febre semitertiana" in the seventeenth century, reports several autopsies in which the small intestine was inflamed, and the lower

part of the ileum in many cases showed spots of sloughing. He did not consider the intestinal lesion as responsible for the symptoms, but thought that they were due to the presence of a putrid substance in the veins. Baglivi and Lancisi at about the same time noted the connection between the intestinal lesions and attacks of the fever. About the middle of the same century Willis in England discussed the intestinal lesions and compared them to the eruption upon the skin produced by smallpox. Hoffmann, of Halle, at this time wrote a good clinical account of a group of febrile cases which had the ordinary characteristics of typhoid, including the characteristic eruption, and he said that after death gangrene and sloughing of the small intestine were found. Sydenham also gave a picture of a fever lasting from fourteen to thirty days with great tendency to diarrhœa, delirium, and epistaxis. Panarolus, at the close of the century, reported many fatal cases of fever at Rome in which the intestines at autopsy appeared as if burned.

These and other accounts written in various parts of the Continent as well as in England during the seventeenth century, with clinical descriptions and accounts of autopsies, leave no doubt that typhoid was then widely spread throughout the civilized world. In the eighteenth century the descriptions become more complete. The report of a case by Morgagni describes not only the ulcers, but perforations in the lower part of the ileum and the first part of the colon, and he further calls attention to the swelling of the mesenteric glands and the spleen. In his letters he several times alludes to cases of what was called double tertian fever, which showed at the autopsy the lesions of the lower part of the ileum and the mesenteric glands. In the middle of the eighteenth century, Tissot describes a bilious epidemic fever at Lausanne, giving a good account of a typhoid epidemic. "In these cases there was first a lassitude, a loathing of food, and a sensation of cold; the patients were drowsy, their tongues foul with a whitish-yellow covering; at times there was sweating, but without the placid interval which succeeds the sweat of true intermittents. There were frequent complaints of the head in the first days; the pulse was weak and about 100; there were daily exacerbations, though these were sometimes slight; the bowels at first were bound, later lax; in the more severe cases fever was higher, the pulse more frequent, the headaches more severe; the sleep was turbulent with anxiety and not at all refreshing. In the worst cases, on the sixth, seventh, or eighth day, a very frequent pulse, delirium, and flatulent swelling of the abdomen, the paroxysms without regularity, a general subsultus of the tendons; the delirium sometimes almost a frenzy, in other cases resembling a lethargy; the stools were irregular and fluid. In five cases there

were purple spots, and these cases were all fatal. In some fatal cases there were hemorrhages. Those who died did so as a rule between the seventeenth and twenty-fifth days. Two cases died after the thirty-fifth day." Huxham's picture of slow, nervous fever given at almost the same time is also interesting. "The patient at first grows somewhat listless and feels slight chills and sudors with uncertain flushes of heat and a kind of weariness all over. This is always attended with a heaviness and dejection of spirit. A nausea and disrelish of everything soon follow. Though a kind of lucid interval of several hours sometimes intervenes, yet the symptoms return with aggravation, especially towards night; the head grows more heavy, the heat is greater, the pulse quicker; a great torpor or obtuse pain affects the head and is commonly succeeded by some degree of delirium. In this condition the patient often continues for five or six days, seeming not very sick; about the seventh or eighth day the giddiness, pain, or heaviness of the head become much greater, often delirium appears with universal tremors and muttering, the tongue grows often very dry, often very thin stools are discharged; now nature sinks apace; the pulse may be said to tremble and flutter rather than to beat; the sick man becomes quite insensible; and the delirium ends in a profound coma, and that soon in an eternal sleep."

In this country an excellent clinical description of typhoid fever was published in 1824 by Dr. Nathan Smith, professor of the theory and practice of physic and surgery in Yale College. He says: "We have reason to believe from imperfect and broken accounts and from oral tradition that it was not long after the first settlement of the country before the inhabitants were afflicted with what is now known as typhus fever, but which was then known as low, long, slow, nervous fever, etc. I have every reason to believe that it has prevailed in every part of the United States." His description of the symptoms leaves no doubt that the fever with which he was dealing and which he spoke of as typhus was true typhoid.

The above facts do not permit us to doubt that this disease has been one of the formidable enemies of the human race from the dawn of history, nor is it limited in its field of activity by geographical boundaries. As Pepper says, "There is no country, whether civilized or not, of which we have any knowledge, in which the disease has not occasionally made its appearance." And while it is more prevalent in the temperate regions than in the very cold or the very hot, still "it is met in every variety of climate; it is endemic in North America, attacking alike the inhabitants of Greenland, British America, and Mexico; it prevails at times in every State in the Union; frequently in Central America and the West Indian Islands; in Aus-

tralia, Great Britain, and Ireland; in every country of Europe; there is evidence that it has prevailed at various times in all the different countries of Asia, Africa, and Australia."

Recognition of Typhoid Fever as a Distinct Disease.—The earlier observers and writers in regard to fevers, even those who from time to time noted the ulcers in the ileum, did not really distinguish as a sharply outlined group, either upon clinical or anatomical grounds, the cases which we now call typhoid fever. The early physicians with their imperfect methods of observation, knowing next to nothing of physical examination and having no accurate means of determining the temperature, could hardly be expected to distinguish one from another certain of the infectious diseases which have no conspicuous eruptions on the skin, such as typhoid and typhus, many forms of tuberculosis and many cases of malarial fever. Some of the first reported cases of intestinal lesions in fever were put into that group which went by the name of semitertiana or hemitritæus, but these terms meant little more than daily fever. By the middle of the seventeenth century, however, Willis, in England, drew a distinction between two varieties of fever—one the febris pestilens, and the other a less contagious form of fever without eruption, with longer duration and with an imperfect crisis. Hoffmann, of Halle, not far from that time also distinguished between the febris petechialis vera and the febris petechizans vel spuria, describing under the latter name the ordinary clinical course of typhoid fever, including the characteristic eruption. Sydenham, in the same century, recognized the distinction of these same two groups of fevers. With them began the discussion, which was not ended for two centuries, as to the existence of a real distinction between typhus and typhoid. Strother, in the early part of the eighteenth century, recognized the difference between certain slow fevers, in some cases of which there was ulceration of the bowels, and the cases of typhus which appeared epidemically in the years 1727 to 1729. Among several writers who during the last century maintained this distinction, the work of Huxham, about 1750, is worthy of especial notice from the satisfactory differential picture which he draws of the "putrid malignant fever" and the "slow nervous fever." Before this matter could be settled to the satisfaction of the profession in general some systematic and careful postmortem observations were necessary. An advance in this direction was instituted by Prost, of Paris, at the beginning of this century. He found in the fevers of Paris many cases showing the characteristic ulcerations of typhoid, but he mistook every post-mortem redness of the intestinal canal for inflammation, and regarded the typhoid ulcerations as nothing more than occasional, extreme instances of an intes-

tinal inflammation which he found very commonly in various forms of fever. This idea was carried still further by Broussais, who taught that all fevers have for their essential features a gastroenteritis, a view which delayed the proper conception of the specific differences of the various fevers. In 1813, Pettit and Serres drew a distinction between the intestinal lesions of "fièvre entéro-mésentérique" and those of an ordinary enteritis. They, and some other French writers, spoke of the intestinal lesion as an internal exanthem, carrying out the idea suggested by Willis a century and a half before. To Bretonneau, of Tours, we owe the first realization that the lesions peculiar to one of the prevalent forms of fever were located in the solitary and agminated glands of the ileum, and that the disease depended upon the action of a poison which could be communicated. Trousseau, in 1826, was the first to put on record the views of Bretonneau. He says: "The long and useful labors of Dr. Bretonneau have finally cleared up this question. Since 1813 he has collected a great quantity of facts, both in his own practice and in the hospital of Tours. He has been led to distinguish a disease, the seat of which seems to be exclusively in the glands of Peyer and the solitary glands which are found in the ileum, the jejunum, and the large intestine. He has given to this affection the name of 'dothinentérie' or 'dothinentérite' from the Greek δοθιήν, pustule, and ἔντερον, intestine." Bretonneau not only recognized the site of the lesions, but the fact that these organs of Peyer undergo a pathological change, the stages of which come on in regular order. Trousseau gives a detailed description of the post-mortem appearances of these portions of the intestine which hardly calls for alteration or addition at the present day. Louis, in his lectures, elaborated the views of Bretonneau. These characteristic lesions were recognized at once in England and in America. In 1827, Dr. Bright published excellent colored drawings of the intestinal lesions. Dr. E. E. Hale, Jr., of Boston, published in 1833 an account of three autopsies of persons considered by him to have died of this disease. If the diagnosis in these cases could be looked upon as certain and positive, they would probably constitute the first published examples of the intestinal lesion of the disease as it occurs in New England. The diagnosis, however, in all three instances must be regarded as somewhat doubtful, and the alteration of the intestinal follicles does not seem to have been very clearly or strongly marked.

The earliest American records of unequivocal cases are probably those of two cases published by Dr. Gerhard in *The American Journal of the Medical Sciences* for February, 1835. In *The Medical Magazine* for June, 1835, Bartlett gave a short account of the enteromesenteric

alterations in five undoubted cases of typhoid fever, alterations corresponding exactly to those described by Louis.

Dr. James Jackson, Jr., of Boston, observed the intestinal lesion in a clear case of the disease as early as October, 1830, although the result of the observation was not made public until 1835. Having studied typhoid fever in Paris, aided and guided by the personal instructions of Louis, he again saw the disease in Boston, and in two cases, one of which occurred in 1833 and the other in 1834, he found the characteristic lesion of the intestinal follicles and mesenteric glands. An account of these observations was published in 1835.

The lesions of typhoid having thus been clearly recognized and carefully studied, the question of the essential distinction of typhoid from other fevers, and especially from typhus, could be more satisfactorily discussed; though, as has been seen, such a distinction had been suggested and at various times insisted upon during nearly two centuries, it was still maintained on many sides that the distinction did not truly exist, and even to the middle of this century many physicians believed that typhoid and typhus were the same disease and that the intestinal lesions were merely an occasional complication. In June, 1836, Dr. Lombard, physician to the Geneva Hospital, wrote expressing his great surprise at his failure, in Glasgow and Dublin, to find in the cases which he dissected any of the characteristic lesions which he had never failed to find in his autopsies of "typhus fever" cases at Geneva and Paris. "In the whole course of my experience I have met with nothing which has surprised me more than this occurrence. I had been engaged for years in the study of typhus fever, and for years my almost daily experience in the dead-room led me to associate certain lesions of the alimentary canal with the symptoms of this disease, when suddenly I find myself assailed with new experiences exactly contradictory of my former." In discussing the matter he points out some differences between the clinical pictures of typhus as he had seen it on the Continent and as he now found it in Dublin and Glasgow, particularly in the eruptions, the diarrhœa, the different degrees of contagiousness, and the different liability of the aged and infants. He is not yet ready, however, to allow that they are specifically distinct, and renounces the opinion that the local changes of structure are of paramount importance in causing or producing the symptoms. In a second letter, dated July 18th, 1836, after further studying the typhus fevers in Liverpool, Manchester, Birmingham, and London, he concludes that the fever observed in Europe is also to be found in the British empire, thus seeming to admit the difference of the two.

America is entitled to the honor of having, through Gerhard, of

Philadelphia, first clearly recognized and fully set forth the distinction of these two diseases. Valleix, of Paris, frankly stated, in 1839, that "Gerhard established for the first time the very important fact that there can exist, and that there do exist, at the same time and in the same country two diseases that may be clearly distinguished and in which one can predict during life the lesions which will be found after death. These diseases are typhoid fever and true typhus." During a residence of two or three years in Paris, Gerhard had studied with great care the pathology of the disease usually termed in the French hospitals typhoid fever or typhoid affection. He had also observed cases of typhus fever which were under the care of Dr. Gregory, of the Edinburgh Infirmary. He was assisted by Dr. Pennock, who had studied typhoid fever in the wards of La Pitié in Paris. And in the year 1835 he related a case of typhoid fever associated with ulcerations of Peyer's patches. At that time he evidently looked upon typhus and typhoid as the same disease, but in 1836 he had the opportunity of studying an outbreak of true typhus in Philadelphia, and in 1837 published an account of this outbreak and clearly established the distinction of the two diseases. He showed that the lesions of Peyer's patches and mesenteric glands, invariably present in typhoid, were never seen in typhus. He insisted on the marked difference between the petechial eruption of typhus and the rose-colored spots of typhoid, and he pointed out that, while the former was decidedly contagious, the latter was not often communicated. He claimed that the epidemic brought by Napoleon's troops returning from Germany in 1813–14, though considered by the leading French authorities as identical with the prevailing typhoid, was really a fever distinct from that and should be classed among the forms distinguished by the term typhus gravior petechialis, or spotted fever. He announced the identity of the typhus of Philadelphia with the jail, camp, and hospital fever of Great Britain.

Stillé, of Philadelphia, and Shattuck, of Boston, contributed largely to the recognition, especially in Paris, of the distinction between the two diseases. Stillé had been house physician to Gerhard in Philadelphia in 1836, and he afterwards studied typhoid fever in Paris. Shattuck worked at this subject under Louis at Paris, and at his request visited the London Fever Hospital to study the disease in England. He there recognized two distinct diseases and presented to the Société Médicale d'Observation in tabular form, and with much minuteness, the points of difference. These views were supported by many writers in different countries, but were by no means accepted by all. Davidson, in the Thackeray prize essay on fever in 1840, and Walters, in 1849, insisted upon the identity of the two diseases, and

they perhaps represented the general belief of the profession both in England and in France. Sir William Jenner's researches, however, published in 1849–51, accomplished the conversion of the medical world to the correct view. Jenner was undoubtedly helped in his work by the fact that in 1847 he himself went through an attack of typhus, and three or four years later an attack of typhoid. Jenner's work included observations on the difference presented by the modes of onset in the two diseases, the character of the eruption, the appearance of the face, the amount of prostration, the epistaxis, the injection of the conjunctivæ, the intestinal hemorrhages, the ulcerations of the larynx and pharynx and œsophagus, the ulcerations of the intestine and gall-bladder, the changes in the mesenteric glands and spleen, and several other points of less importance or less constancy; but the main feature of his proof, based upon his careful observation of epidemics and the transmission of the diseases, was the demonstration that the poison of typhus fever or typhoid fever in every case only produced the same disease.

ETIOLOGY.

The doctrine of the etiology of typhoid fever has undergone a complete change since the confirmation of the suspicion, long entertained, that the disease is spread through the agency of a contagium vivum, a microorganism, and the discussion of this branch of the subject has been thereby greatly simplified.

Predisposing Causes.

Age.—Of all the predisposing causes of typhoid fever, age is the most prominent, and its importance can scarcely be overestimated. While it cannot be said that any age is wholly exempt, the occurrence of typhoid fever is extremely rare at the extremes of life. It is preeminently a disease of youth, by far the larger proportion of those attacked by it being between the ages of ten and fifty years—this statement holding good of all countries. Some observers approximate the limits still further and contend that the great majority of patients are between the ages of fifteen and thirty. At one time it was believed that young children were not subject to typhoid fever; but Trousseau and others have shown that even infants under one year of age are not exempt from infection.

Murchison, whose experience at the London Fever Hospital extended over a period of twenty-three years, gives the following statistics of the ages of typhoid patients during that time: Of 5,911 cases

admitted between the years 1848–70, 56.70 per cent. were between fifteen and thirty years, 28.58 per cent. were under fifteen, 13.30 per cent. were over thirty, while only 1 in 71 cases exceeded fifty. Liebermeister found that 77 per cent. of the typhoid patients in the hospital at Basle from 1865 to 1870 were between fifteen and thirty years of age, and Fiedler, in Dresden, found the same limits of ages in 81 per cent. of typhoid patients. In a table prepared by Curschmann, showing the prevalence of typhoid fever at various ages, we find the greatest number of cases at the eighteenth year, the curve falling very steadily and evenly from that age to sixty, from which age to eighty it forms nearly a horizontal line. Of 432 cases occurring in Stockholm from 1867 to 1877, the greatest number was found between eighteen and twenty-eight years, the maximum being at the age of twenty-three years. Very few cases occurred in children under eight years of age, and almost none in persons over forty-five years. Almost exactly parallel with this is the curve of deaths from typhoid fever in Paris in the decade of 1880–89. The greatest number of deaths occurred at the age of twenty-three years, and a very large proportion of the total between eighteen and twenty-eight years. In a table prepared by H. E. Smith, showing the ages at which death occurred in 5,180 cases during the fifteen years from 1880 to 1894 inclusive, in Connecticut, we find again the greatest number of fatal cases between the ages of twenty and thirty years.

Sex.—Judging from hospital statistics alone, it would seem that males are slightly more liable to contract the disease than females. Thus there were admitted into the Metropolitan Asylum Board's hospitals in the years 1871–92, 3,293 males and 3,030 females between the ages of ten and thirty-five years. But when it is considered that men are more often inmates of hospitals than women, this fact loses most of its significance, and the truth probably is that, so far as susceptibility to typhoid fever is concerned, the sexes are upon the same plane. It has been argued that the disease is more fatal to women than men, and hospital statistics have been brought forward to bear out the statement; but it is very doubtful whether a careful study of the figures would confirm this.

Social Position and Occupation.—Typhoid fever exhibits a marked predilection for the well-to-do and cultivated classes of the community. The truth of this remark has been emphasized on many occasions, but the explanation of it is not easy to give. The arrangement of bath-rooms and water-closets in too close proximity to the bedrooms in the houses of the well-to-do has been alleged as a reason by some authors. The influence of occupation in predisposing to typhoid does not appear to be great. Murchison drew attention to an interest-

ing point, that persons moving from one locality to another, or even from one house to another in the same neighborhood, were frequently attacked by the disease, and stated in support of his assertion that of the typhoid patients in the London Fever Hospital, more than six per cent. had been in London but three months. Trousseau noticed that visitors to Paris were more liable to typhoid infection than the natives, and the experience of those who have studied the subject in places where typhoid is rife is in agreement with these observations.

Season.—Typhoid fever prevails probably to the greatest extent in the United States, Canada, in some parts of the European continent, and in Great Britain. The disease is, however, by no means confined to the northern temperate zone, but rages with more or less virulence in almost every part of the globe. The months in which it prevails most in the northern temperate zone are the last six months of the year, from July to December; and in the southern temperate zone, from February to July. Statistical testimony shows that in the fall of the year, in September, October, and November, the inroads of typhoid are the most widespread and severe. Of Murchison's 5,911 cases at the London Fever Hospital in twenty-three years, 27.7 per cent. of the entire number were admitted in the months of October and November, and only 7.3 per cent. in the months of April and May. Hence comes the term "autumnal fever," by which name typhoid was formerly known in some regions. In those cities where the hygienic arrangements have been long defective and where the water supply is polluted typhoid fever frequently becomes endemic.

Whether the level of the ground water exercises any influence in the dissemination of typhoid is more than doubtful, and observations made to clear up this point have almost invariably had a negative result. Pettenkofer showed that in Munich there was a certain inverse relation between the height of the ground water and the prevalence of typhoid fever; that in the years when the ground water was lowest the typhoid death rate was highest. But after 1881 this correspondence disappeared. Observations made in other cities have some of them shown no correspondence, and others quite the reverse relation. The disappearance of typhoid fever, which has been almost complete in Munich since 1881 without any important change in the supply of drinking-water, has been attributed to the clearing of the soil by canalization and to the establishment of the new slaughter-house. Even granting that von Pettenkofer established the fact of a very close relationship between the level of the ground water and the prevalence of typhoid fever in Munich, it was an isolated case and does not apply to other cities. In connection with Pettenkofer's observations the interesting point may be noted that after he had

satisfied himself of the relationship between typhoid and the level of the ground water, his interpretation of the causation of the disease was that drinking the water had nothing to do with it, but that it was caused by breathing typhoid-germ-laden air forced out of the ground by fluctuations of atmospheric pressure.

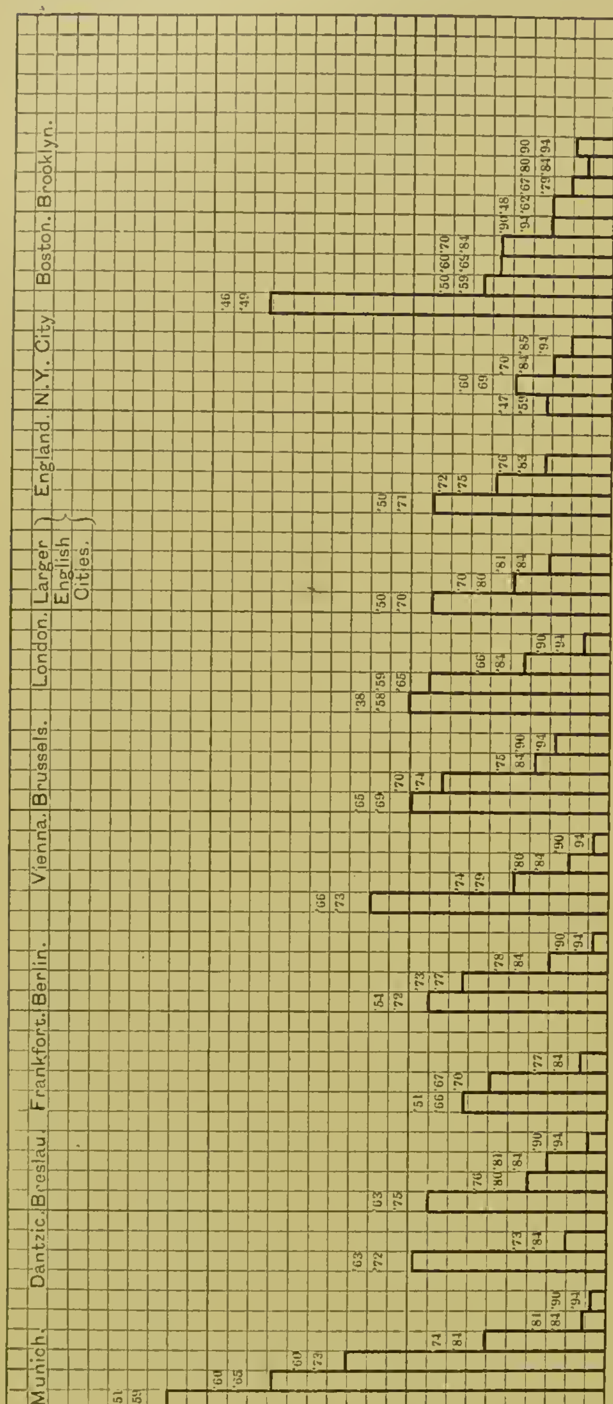

CHART No. 1.—Showing the Reduction in the Mortality Rate from Typhoid Fever Effected by Improved Public Hygiene. The figures show the number of deaths from typhoid fever in each 10,000 inhabitants in a number of cities in different parts of the world, before, during, and since the introduction of an efficient sewerage system and of an adequate water supply. (W. C. Deming.)

That inhaling sewer gas may occasion typhoid has long been the contention of some; but it has been proved by Miguel, Haldane, Laws, and others that sewer air is remarkably free from germs, and Laws asserts that the bacillus coli communis has never been found in sewer air, although it is plentiful in sewerage.

Moisture and temperature were once believed to be very closely and constantly related to an epidemic prevalence of typhoid. This view is now, however, to a large extent discredited, and probably the majority of observers hold that, whether the foregoing season be wet or dry, it makes but little difference to the activity of typhoid. Murchison thought that warm, moist, but

not rainy weather was likely to be followed by a prevalence of typhoid fever.

Physical and mental fatigue and intemperance are not predisposing causes to typhoid, except in so far that they lower the powers of resistance against infection.

Unsanitary Conditions.—The old-time view that typhoid fever was solely and essentially a filth disease has been wholly exploded, and still the incontrovertible fact remains that filth is a most important factor in its causation. The filth is the nidus in which the germ finds a suitable breeding-place. Polluted water is the *fons et origo* of the typhoid evil. It is not true that all sewage-defiled water always contains the typhoid poison; but it is true that such water is more likely to do so than water not thus contaminated. This fact is so well known, and has been so conclusively demonstrated in whatever places adequate water supplies and efficient sewer systems have been introduced, that it would be superfluous to multiply instances.

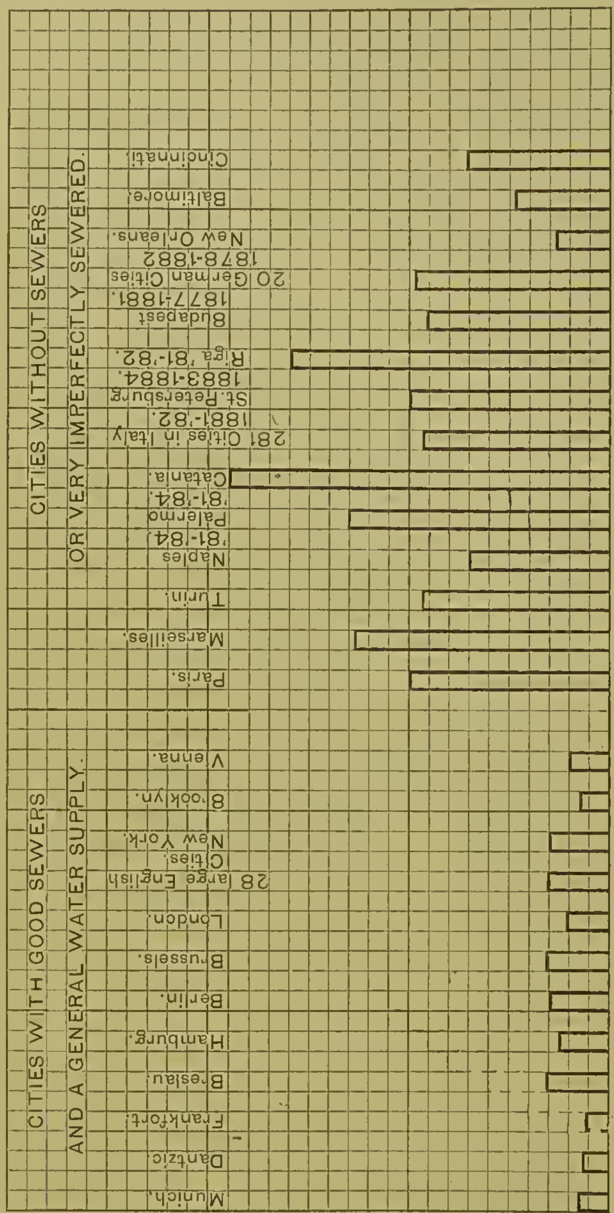

CHART No. 2.—Showing the Comparatively Low Mortality from Typhoid Fever in Cities Properly Sewered and having an Adequate Water Supply. (W. C. Deming.)

The accompanying charts show the reduction in the typhoid mortality rate brought by proper sanitary measures and a pure water supply.

Immunity, Acquired and Natural.—A person who has had one at-

tack of typhoid fever is generally immune. Of two thousand cases of enteric fever at the Hamburg General Hospital, only fourteen persons were affected twice, and only one person three times. There are, nevertheless, instances well authenticated of the same person having passed through several attacks of typhoid fever. Immunity may be in some degree acquired, even without a previous attack of the disease. Those habitually exposed to the poison appear to be more or less proof against infection, especially those in feeble health. It cannot be denied that races exist the members of which do not enjoy absolute immunity from typhoid, yet who are so seldom attacked by it that they may be termed practically immune. The inhabitants of the Orient are perhaps the most striking examples of this acquired immunity. The natives of the foul, overcrowded cities of India rarely, if ever, suffer from typhoid fever, and the same may be said of natives of the East generally. At a meeting of the French Academy of Medicine, held on May 10, 1898, Vincent of Val-de-Grâce said that he had found that French soldiers in Algeria were on an average a hundred times more subject to typhoid fever than native soldiers—a noteworthy observation, because the disease is in general serious when it attacks Arabs. The comparative exemption of the Arab depends, in Vincent's opinion, neither on a previous attack nor on a slow acclimatization consequent on residence in towns, but rather on the possession of a natural immunity, comparable to the immunity of negroes against yellow fever. He endeavored to determine whether the blood obtained from Arabs caused agglutination of typhoid bacilli, and examined the blood of twenty-three natives with that end in view, but it presented no distinct reaction.

Some chronic diseases are supposed to confer a certain immunity, notably phthisis, while pregnancy and lactation are credited with a like effect.

Bacteriology.

It is now about thirty years since little clusters of microoganisms were first observed in the tissues in fatal cases of typhoid fever. During the first decade of this period the methods of study were so crude and the observations had so little in common that they have now only a passing historical interest. Among the early discoverers whose observations are on record were Recklinghausen (who was the first to report, in 1871, the interesting fact of colonies of microbes in miliary abscesses of the kidney in the course of typhoid fever), Eberth, Klein, Browicz, Sokoloff, and Fischel. The majority of these discoverers were inclined to consider the presence of the micro-

organisms as secondary. Scientific interest begins with the second decade, and we can say that we owe to Eberth the first definite ideas in regard to the pathogenic bacillus of typhoid fever (1880–82). Studying by means of sections cleared by acetic acid the spleen, the lymph nodes, Peyer's patches, the liver, kidneys, and lungs in twenty-three typhoid cases, he found in the lymph nodes and in the spleen clusters of microbes. Later by staining with methyl violet, he demonstrated the presence of microbes in scrapings from the spleen and lymph nodes of typhoid cases. Being unable to find any such micro-organisms in other diseases, even when complicated with intestinal lesions, he claimed a specific relation to typhoid fever for the bacillus he had discovered. Photomicrographs taken by Koch at the same time, and independently of Eberth, show that he had observed this same bacillus in the liver, spleen, and kidneys in cases of typhoid fever. The discovery of Eberth was also confirmed by Meyer in Germany and by Coates and Crooke in England. A valuable contribution to the study of Eberth's bacillus was made by Gaffky, who, in 1884, first obtained it in pure culture in gelatin and on various other culture media. Gaffky, moreover, made a complete study of this micro-organism in which he reviewed its characters of morphology, distribution in the body, and experimental reactions in animals. He was unable to prove conclusively its pathogenic nature. Subsequent study has detected few errors in Gaffky's observations, but has generally confirmed them. Many facts, however, have been added in regard to the identification, biology, and pathogenic properties of this bacillus. One of the most striking features of its subsequent history is the attempt made by Roux and Rodet to identify the colon bacillus and the bacillus of Eberth—an attempt which aimed at nothing less than to rob the typhoid bacillus of all specific character and to reëstablish on a biological basis the theories of Murchison. The contest has been active, and numerous works have appeared on this question. As a result the autonomy of the bacillus of Eberth is fully established, but many points which seemed to be proved by the older works must be revised on the basis of later discoveries.

Morphology.—The typhoid bacillus is seen in the form of very motile, slender rods 1 to 3 μ long by 0.5 to 0.8 μ thick, sometimes growing out into pseudofilaments. The size of the rods varies considerably in specimens obtained from different sources. The bacilli from agar cultures, grown at blood temperature, and from the tissues of animals and human beings appear smaller in all dimensions than when grown on gelatin and potato, on which media, especially at low temperatures, they frequently take the form of long threads. The single rods are straight, regular in outline, and with blunt but rounded extremi-

ties. In stained specimens from cultures they are often slightly curved. The bacilli from old cultures also often appear somewhat irregular in shape.

The typhoid bacillus is readily stained with all of the common aniline dyes, but easily parts with its color when treated with decolorizing agents—*e.g.*, the iodine solution of Gram. It is somewhat more difficult to stain than most bacteria, but there is no constant difference between it and the other bacteria of the same group in this respect. Refractive granules are not infrequently seen at the poles of the bacilli, especially in potato cultures. These are readily and intensely stained by aniline colors. There may also be vacuoles, situated at the poles or centrally or along the sides of the rods, which remain unstained. These appearances are not due to spore formation but to retrogressive changes, for the cultures in question have less power of resistance than those of the usual type. Although Gaffky and others at first announced the discovery of spore formation, subsequent investigation has not substantiated their claim. The existence of spores has more recently been asserted again by Almquist. From his description they would appear to be quite different from true endogenous spores, but in regard to their power of resistance no experiments were cited. The movements of the typhoid bacilli may be described in the case of the smaller individuals as rapidly swinging and tumbling in character, the larger bacilli progressing in a more serpentine manner, which is most pronounced but slower in the longer threads. They propel themselves by means of a number (ten to eighteen) of flagella which are distributed over the entire surface of the cell. These appear as slender, sinuous threads from three to five times as long as the bacilli. They can be stained and demonstrated by the method of Löffler, who recommends a solution of tannin and ferrous sulphate as a mordant, to which is added a certain proportion of a one-per-cent. solution of caustic soda with fuchsin or methyl violet.

Biology.—The typhoid bacillus grows readily in a variety of culture media at the "room temperature," very scantily at from 9° to 15° C., and most abundantly at the body temperature (37° C.). Its development is impeded at 42° C. The presence of oxygen is advantagous but not necessary. It grows rapidly in gelatin without producing liquefaction. Superficial colonies in gelatin, early in their development, have a somewhat characteristic appearance. They are transparent, iridescent, and have an irregular outline which is compared to that of a grape leaf. Deep colonies are spheroidal and of a yellowish color, gradually changing to brown. Cultures in bouillon give it a uniformly cloudy appearance. No pellicle is formed on the surface. On potato the appearance of the growth is variable according as the reaction of the

potato is acid or alkaline. The appearance described by Gaffky may be considered as typical. This consists of an invisible growth covering the entire surface and causing a smooth, glistening appearance. At times the growth is more luxuriant and of a yellowish or brownish color, resembling an ordinary culture of the colon bacillus. The typhoid bacillus grows feebly or not at all in solutions containing asparagin. It does not produce indol in solutions of peptone or in bouillon, nor does it cause fermentation of grape, milk, or cane sugar. It causes the formation of acid from grape sugar, but no gas. It grows readily in milk, producing a slightly acid reaction, but does not cause coagulation. Media containing no sugar gradually become strongly alkaline.

In regard to its power of reduction observations vary. According to Germano and Maurea, only a slight reduction of indigo sulphate of sodium takes place regularly in case of agar stab cultures, whereas the great majority of the members of the colon group are powerful reducing agents. Lösener states that there is only a slight difference in this respect. Nitrates are reduced to nitrites, and sulphide of hydrogen is evolved, but less energetically than in the case of numerous other bacteria. Hugonneng and Doyen found that both the typhoid and colon bacilli set free nitrogen in peptone solutions containing 1.5 per cent. of sodium or potassium nitrate. They are very similar in this respect, in both the degree and rapidity of the reaction. No pigment is formed by the typhoid bacillus. The cultures are found to contain toxins, and when cleared by filtration of living bacteria these produce marked symptoms of poisoning in animals.

Distribution.—The typhoid bacillus is found in certain conditions in the soil and in water, but so far as known only when these are contaminated by the discharges from typhoid-fever patients. Recently Lösener claimed to have discovered in five instances typhoid bacilli in soil and in tissues and fæces in which there had been no suspicion of their presence. They have never been demonstrated in the healthy human body. During the course of typhoid fever they are widely distributed through the body and in the excreta. Cultures are obtained most easily and surely from the spleen and lymph nodes of the mesentery, in which the bacilli are constantly found scattered about in little clusters. This arrangement in scattered clusters is characteristic, and as a rule it is only in the walls of the intestine that they are observed singly or in loose chains following the course of the lymph vessels. There can be no question that the groups of bacilli are formed during life. The proof of this fact, according to Flügge and others, consists in evidences of retrogressive changes in the rods as shown by a poor reaction to stains. On the other hand, there is a

possibility that the bacilli proliferate also after death (Fraenkel, Simmonds, and others). This distribution in the tissues, although characteristic, is not peculiar to the typhoid bacillus, for the colon bacilli may be found similarly grouped. The typhoid bacilli show a preference for the lymphatic system, choosing first the solitary and agminated glands of the intestine, then the mesenteric lymph nodes, and lastly the spleen. The liver and the kidneys are invaded to a less extent. It is said that they can almost always be found in the marrow of the bones (Quincke and Stuhlen). The distribution of the bacilli in the body can be explained only by the theory that they enter the general circulation. This theory has also been confirmed by the direct examination of the blood. It is true that not all have been successful in such examinations (Gaffky, Janowski, Grawitz), and some may have been deceived by contaminations with similar bacilli, but many positive results can be cited. R. Stern obtained the typhoid bacillus in 3 out of 6 cases, twice in blood from rose spots, and once in that from a vein. Banti succeeded in 1 of 2 cases. Neuhaus, in blood from rose spots, obtained cultures in 9 out of 15 cases examined. Fraenkel and Simmonds, in 6 cases, found the bacillus once. Thiemich, examining the blood of 7 cases, drawn both from veins and from rose spots, obtained a growth of typhoid bacilli 3 times from the rose spots and once from a vein. The results obtained by Kühnau are perhaps the most free from error. In 41 cases he examined blood taken from a vein with elaborate antiseptic precautions, and in 9 cases he obtained a growth of typhoid bacilli. By a simpler method of vein puncture, and using a smaller quantity of blood, James and Tuttle succeeded 3 times in 38 cases.

The bacilli can, of course, be carried by the blood current to all parts of the body, and they may be deposited in the central nervous system. Curschmann has reported a case in which he found them in the white substance of the spinal cord, distributed for the most part singly rather than in groups. This observation has not yet been confirmed. The case presented symptoms resembling those of Landry's paralysis, and the spinal cord showed only unimportant histological changes.

The typhoid bacilli can also pass from the maternal circulation to the fœtus (Neuhaus, Eberth, E. Fraenkel and Kiderlen, Hildebrandt, and others). Frascani, in experiments on animals, was regularly able to demonstrate the bacilli in the fœtus. He finds the explanation of this in the hemorrhages of the placenta, which may occur both in animals and in human beings.

The presence of the bacilli in the fæces of typhoid patients has

been repeatedly demonstrated by many bacteriologists. It is probable that they are not evenly distributed through the fæces, and they are most abundant during the period of active intestinal ulceration. The failure to demonstrate their presence at any given time in the disease cannot be considered proof positive of their absence. The identification of the typhoid bacillus in fæces is difficult at the best, and in the multitude of other similar bacteria it may easily escape detection. The most promising methods of examination are given below.

It is very often present in the urine also, appearing probably somewhat later than in the fæces. Neumann obtained typhoid bacilli in cultures from the urine in eleven out of forty-eight cases and Karlinski in twenty-one out of forty-four cases (once as early as the third day). Slight changes in the kidneys always take place in typhoid fever, and many cases reported show that they may be of a serious nature.

Typhoid bacilli do not often appear in the sweat, but Geisler claims to have found them in one instance.

The assertion made by Sicard, that they may be present in the expired breath, is improbable. The discovery, by Lucatello, of typhoid bacilli in saliva and in the mucous membrane of the larynx has not been confirmed.

According to Chiari, typhoid bacilli are almost always present in the gall-bladder (in nineteen out of twenty-two cases). Others also have reported their presence in this situation. How they reach the gall-bladder has not yet been demonstrated.

Histological changes in the tissues immediately surrounding the groups of bacilli have not been noted. Many cases have been reported, however, in which typhoid bacilli have acted as the exciting causes of inflammation and pus formation, and their power in this respect has been proven by experiments on animals. A. Fraenkel reported an encapsulated focus of pus in the peritoneum. Weichselbaum saw a case of general peritonitis following rupture of the spleen. Many have reported suppurative processes connected with the bones, such as osteomyelitis or periostitis. Typhoid bacilli have also been obtained in pure culture in typhoid pneumonia, in serous and suppurative pleurisies, and in cases of suppurative meningitis. There is, however, no reason for assuming a specific typhoid form of inflammation and suppuration (Flügge). It is possible that other bacteria, after having assisted in the production of these processes, have disappeared from the field.

Identification of the Typhoid Bacillus.—The positive identification of the typhoid bacillus is a matter of the highest importance, and perhaps as difficult as it is important. Many problems relating to

public hygiene, food and water supply, clinical diagnosis, and pathology depend for their solution upon a thorough knowledge of this bacillus and practical methods for its positive identification.

Before the publication of Gaffky's investigations, in 1884, microscopical appearances and certain staining peculiarities were depended upon for the recognition of the typhoid bacillus. Since that time, improved methods of study and many important discoveries have shown that the morphology and staining properties of this bacillus are not sufficient to identify it and, indeed, are of comparatively slight importance. Brieger, in 1884, Emmerich, in 1885, and Escherich, in 1886, discovered in human fæces certain microorganisms which, although given different names by their discoverers, were probably identical, or at least varieties of one species. The name given by Escherich to the organism isolated by him, Bacterium coli commune, has been retained in slightly altered form—viz., Bacillus coli communis or colon bacillus. The study of this bacillus by different bacteriologists seems to show that the term colon bacillus applies to a species which comprises many varieties of similar bacilli, but which are distinguished from each other by slight biological and microchemical differences. The colon bacilli in general closely resemble the typhoid bacillus in form, size, staining properties, biological characteristics, and pathogenic effects in certain of the lower animals. The distribution and arrangement of these bacilli in the tissues are practically the same as in the case of the typhoid bacillus. They are found constantly in the intestinal canal and fæces of human beings and in those of many, if not all, of the lower animals. The problem, then, which has occupied the attention of bacteriologists for the past fifteen years has been to find a sure and rapid method of distinguishing the typhoid bacillus from the different varieties of the colon bacilli and such other bacilli as in any way resemble it. The slight difference in size may be disregarded as it is not constant and practically not appreciable. The distinguishing features which are relied upon to identify the typhoid bacillus are as follows:

1. They are slender bacilli which grow in gelatin without producing liquefaction and present a somewhat characteristic appearance in young colonies upon the surface. When stained, they are readily decolorized by Gram's method.

2. The typhoid bacillus grows less rapidly and luxuriantly on all culture media than the colon bacilli.

3. It regularly possesses a greater number (ten to eighteen) of flagella than the colon bacillus (four to eight). It is also more actively motile. Indeed, except in very recent young cultures, the colon bacillus shows very little and often no motility.

4. The growth of the typhoid bacillus upon potato is invisible, while that of the colon bacillus is conspicuous and of a dirty-yellowish color. This difference, however, is not constant and is unreliable. According to Germano and Maurea, if the suspected bacillus is planted on one half of a potato and on the other half a known pure culture of the typhoid bacillus, the slightest essential difference between the two growths proves the bacilli to be different.

5. The typhoid bacillus does not produce indol in peptone solutions.

6. It does not coagulate milk.

7. It does not produce gas in lactose or glucose bouillon.

The colon bacillus coagulates milk and produces gas and indol under like conditions.

Another difference emphasized by Lösener is the stronger acid reaction produced in a certain medium by the colon bacillus. At the end of forty-eight hours the amount of acid is more than twice that produced by the typhoid bacillus.

No single one of the above tests is sufficient to distinguish the typhoid bacillus from all varieties of the colon bacillus. It is only by the concurrence of all of these tests, compared in each instance with a like test of a known culture of typhoid bacilli, that we can positively identify a suspected bacillus as the typhoid bacillus. The results of animal inoculations are so varied and so little characteristic that such experiments are practically useless in determining the identity of the typhoid bacillus. The experiments of Pfeiffer and Kolle, however, have demonstrated that animals which have been rendered immune to typhoid fever are as susceptible as usual to the other bacteria of this group—*e.g.*, to the colon bacillus. The serum of the immunized animals, sometimes in a dose of only a few milligrams, acts as a protection against typhoid bacilli only and not against the colon bacilli, and vice versa. We may hope, from these facts, to be able by this method of specific immunization to differentiate the typhoid bacillus from other bacteria when all other means fail. Instead of insisting upon the employment of animals for this purpose it is perhaps allowable to draw diagnostic conclusions, as stated by Pfeiffer and Kolle and others, from the results of planting in pure specific serum or in mixtures of this serum with bouillon (1:40). This medium prohibits the growth of the typhoid bacilli only.

The difficulty in isolating the typhoid bacillus from mixtures, like fæces, containing innumerable bacteria of many varieties, some of them of very rapid growth and causing the liquefaction of gelatin, has led to the invention of many methods aiming to accomplish this. The value of any such method, next to its accuracy, is determined by

its rapidity and simplicity in practice. Most of the methods thus far devised have failed in other hands to accomplish the results claimed for them by the inventors. A medium which will permit the growth of the typhoid bacillus while preventing or greatly retarding the growth of other bacteria, or a medium in which the appearance of the growth of this bacillus is sufficiently characteristic to distinguish it, has been sought. The ability of the typhoid bacillus to grow in slightly acid media and in the presence of certain antiseptic agents has been chiefly relied upon. Unfortunately the bacilli of the colon group possess the same power and even in greater degree. Holz employed a preparation of gelatin in potato juice, to which he added a minute quantity of carbolic acid. The reaction of this medium was slightly acid. Elsner retained the slightly acid potato gelatin of Holz, but in place of carbolic acid added one per cent. of potassium iodide. Upon this medium the typhoid and colon bacilli developed, while the growth of almost all other varieties, especially those producing liquefaction, was inhibited. The growth of the colon bacilli was rapid, the colonies being easily seen at the end of twenty-four hours. On the other hand, the typhoid bacilli grew slowly, so that the colonies were scarcely visible after twenty-four hours, but at the end of forty-eight hours could be easily distinguished by their size and color from those of the colon bacilli. Properly carried out, this method has yielded fairly uniform results. A plate in which the colonies are few and widely separated offers the best conditions for characteristic growth. When the colonies are thickly sown, the development of all is restricted, and the distinguishing features do not appear.

By the use of Elsner's method, Sterling succeeded in isolating the typhoid bacillus in sixty per cent. of the cases examined. He considered it a decided improvement on previous methods. But failure to demonstrate the presence of typhoid bacilli does not exclude the possibility of their presence. Diagnosis depends on a positive result. A negative result is of very little value.

Lösener often succeeded in isolating the typhoid bacillus from fæces by the use of simple gelatin, to which he added .05 per cent. of carbolic acid. After the development of the colonies he transplanted into glucose agar a considerable number of the smaller ones which seemed most likely to be typhoid bacilli. He then subjected to further examination only the cultures in which there was no formation of gas. The length of time required by these methods detracts from their practical utility.

Many other ingenious methods have been devised, among which may be mentioned the colored media of Robin and of Ramond and

those containing urine. The interesting experiments of Klie, also, with media containing different percentages of gelatin deserve mention. By the use of a medium containing 3.3 per cent. of gelatin at 18° to 19° C., he obtained, after from twenty-four to thirty-six hours, a fairly constant type of colonies of both typhoid and colon bacilli. The differences, however, were not sufficiently striking positively to distinguish them. These methods, although most of them are of little practical use, contain many suggestions and hints and have contributed materially to the solution of the problem.

More recently a method devised by Hiss accomplishes the isolation and identification of the typhoid bacillus from fæces with not less accuracy and in shorter time than previous methods. Impressed by the observations of Baginsky, Rosenthal, and Klie in regard to the effects of media of reduced consistence upon the forms of colonies, especially of motile bacteria, Hiss aimed to utilize the facts discovered by them by making a medium which would have a semi-solid consistence at the temperature of the body. This method requires the use of two slightly different media containing both agar and gelatin and having a certain degree of acidity. One is for use in plates and the other for tube cultures. The plate medium contains one per cent. of agar and 2.5 per cent. of gelatin, and is of firmer consistence than the tube medium, which contains only 0.5 per cent. of agar and eight per cent. of gelatin. The degree of acidity of the tube medium is also slightly less. The proper consistence of these media is obtained at incubator temperature (30° to 40° C.), which also favors the rapid development of the bacteria. At the end of sixteen to eighteen hours the development of the colonies in the plates is sufficient to show growth characteristics which are generally distinctly different in the typhoid colonies from those of the colon group. The colonies which present the typhoid characteristics are now transplanted to the tube medium. After from sixteen to eighteen hours in the incubator the entire medium is evenly clouded if the typhoid bacillus is present. On the other hand, none of the colon bacilli produces this appearance. Thus within thirty-six hours it is possible to isolate the typhoid bacillus from fæces with remarkable certainty, as shown by the usual tests. The value of this method has now been pretty thoroughly demonstrated. The importance of strict accuracy in making the media, especially in obtaining the proper degree of acidity, has hindered somewhat the general use of this method.

Persistence in the Body.—A number of observations have been made as to the length of time the typhoid bacilli may persist in the human body after the recovery of the patient. No definite rule can be formulated from these observations, but it seems to be proved that when

placed under favorable conditions the typhoid bacillus may remain alive in the body for months and, if we may believe the statement of one observer, for years. Buschke states that cultures of typhoid bacilli were obtained from an old focus of inflammation in bone seven years after the time of original infection. Sahli demonstrated the presence of typhoid bacilli in a pleuritic exudation fifty days after the beginning of typhoid fever. Orloff, after six and one-half months, found them in the granulation tissue of a focus of periosteal inflammation. Chantemesse found them in the pus of an osteomyelitis nine months after a severe attack of typhoid fever. Werth found them after eight months in the contents of a suppurating ovarian cyst. Valentini, Loriga and Pensuti, and Fasching have found them after various shorter periods. Hinze gives a detailed account of the isolation of typhoid bacilli from the pus of a costal periostitis ten months after the termination of the original disease. In the situations mentioned the bacilli are not only kept from drying and the effects of sunlight and extremes of temperature, but they are also protected against other bacteria.

Resistance.—It is important to know how long typhoid bacilli can live outside of the body. On this point very many observations have been made in widely varying conditions. The fact that spores are not formed by them warrants the assumption that their power of resistance is not greater than that of other non-spore-bearing bacteria. They are destroyed by moderate degrees of heat. Sternberg found an exposure of ten minutes to a temperature of 56° C. sufficient to kill them. Potato cultures containing the refractive granules described by Gaffky as spores were regularly killed by a temperature of 60° C. This observation has been confirmed by Buchner, Janowsky, Pfuhl, and many others. Authors are in accord as to the degree of heat required to destroy with absolute certainty the typhoid bacilli; but the time required at 60° C. is somewhat variably stated. Flügge's text-book recommends an exposure of from one-half to one hour at 60° C., in order to insure their destruction. An exposure to 65° C. for five minutes is also stated to kill them. Long exposure to very low temperatures does not seem to injure their vitality. Prudden found the typhoid bacilli alive after an exposure of more than three months in ice at −11° C.

According to Janowsky, cultures exposed for four to eight hours to direct sunlight are destroyed.

Drying destroys the bacilli with only moderate rapidity. Gaffky and Pfuhl found them to remain alive for three months. Uffelmann, testing them in dried garden earth, white sand, and on linen, buckskin, and wood protected from sunlight, found them alive after from

twenty-one to eighty-two days. But in experiments reported by Flügge and by Paffenholz, they always succumbed within five to fifteen days, when dried in thin layers.

Typhoid bacilli retain their vitality in cultures for months when under favorable conditions. Sternberg found them alive after more than a year.

Observations regarding their vitality in water vary widely. Hochstetter (1887), working with distilled water, found five days to be the maximum duration of life of typhoid bacilli. Strauss and Dubarry found them alive in the sterilized waters of the Ourcq and of the Vanne after eighty-one and forty-three days. Hueppe, in the water of a very impure well, found them alive for thirty days.

The experiments of Jordan with reference to this point are instructive. He found that the age of the culture influences greatly the life of the bacilli placed in water. A freshly isolated culture possesses distinctly greater vitality than one which has been under cultivation several months. In sterilized water from Lake Michigan the typhoid bacillus does not multiply to any extent, but under certain conditions may maintain its vitality for more than ninety-three days. The colon bacillus, under the same conditions, multiplies rapidly and may remain alive more than two hundred and sixty-two days. In distilled water typhoid bacilli perish much more speedily than in water from the lake. Jordan found eighteen days to be the limit of vitality in distilled water for fresh cultures, while old cultures survived less than six days. A minute quantity, even 0.0126 per cent., of organic nitrogenous material causes a perceptible lengthening of life in distilled water, while in sterilized lake water a still smaller quantity suffices. These facts may explain the differences in the results obtained by various authors. The organic matter which may be introduced into the water with the specimen to be tested may be sufficient to prolong the life of the bacilli. In natural conditions other factors (such as sunlight, alternate freezing and thawing, competition with other bacteria, etc.) may influence the vitality of the bacilli. In Flügge's textbook it is stated that as a rule they disappear from water by the end of two weeks, but under favorable conditions they may maintain their vitality for a much longer period.

Uffelmann has shown that typhoid bacilli, planted in fæces from persons in good condition and kept at a temperature of 17° to 20° C., maintain life for more than four months, provided the medium is feebly alkaline.

Investigations with reference to the persistence of typhoid bacilli in soil are less numerous. Grancher and Deschamp have shown that they may remain alive in soil more than five and one-half months.

Karlinski concluded from his researches that they do not live more than three months. He states that they retain their vitality in the deeper layers of the soil longer than upon the surface where they are exposed to the sun. Martin found that in soil which was polluted with organic substances the typhoid bacilli speedily increased and spread abroad; while in virgin soil, under like conditions, they diminished and quickly died out. In black mould both typhoid and colon bacilli maintained their vitality for more than fifteen weeks. In virgin soil no growth whatever occurred. Robertson also tested various soils, some of which he treated with dilute organic solutions, while others were not so treated. The results of his experiments show that typhoid bacilli are capable of growing very rapidly in some soils, and that apparently they can survive from one summer to another. In soil containing no organic matter they did not survive. Cultures planted at a depth of eighteen inches grew to the surface. Those planted on the surface grew downwards only three inches. They did not spread laterally to any extent in his experiments, a result which differed from those observed by others. These experiments seem to show that it is more dangerous to bury the excreta of typhoid patients than it is to spread them upon the surface, where they are exposed to sunlight and drying.

Heim has found the typhoid bacillus planted in milk to live thirty-five days; in butter, twenty-one days; and in cheese, three days. Seitz has found the bacillus to preserve its vitality when immersed for three days in a liquid containing 0.03 per cent. of hydrochloric acid. Strauss and Woertz, working with pure gastric juice or with hydrochloric acid in strength of 0.09 per cent., have found the bacillus to resist this treatment for two hours.

Animal Experiments.—According to our present knowledge, typhoid bacilli have no specific pathogenic action on animals. The numerous attempts which have been made to communicate typhoid fever to the lower animals have failed, we may say, in every instance. A number of writers claim to have succeeded in producing typhoid fever experimentally, because, in rare instances, they have observed ulcerative processes in the intestine and a slowly progressive disease. Birch-Hirschfeld, in 1874, by feeding large quantities of typhoid stools to rabbits, produced in some of them symptoms which in some respects resembled those of typhoid fever. These experiments, however, were repeated by Bahrdt upon ten rabbits with an entirely negative result.

Motchoutkovsky injected blood from typhoid patients into apes, rabbits, dogs, and cats with no better success. Walder fed to various animals both fresh and putrid discharges from typhoid patients

and blood taken from the body after death, without any positive results.

The first experiments with pure cultures of the bacilli were made by Gaffky, who placed them in the food of animals and injected them into the peritoneal cavity and subcutaneously. Five apes were fed daily for a considerable time with pure cultures of the bacilli, and the temperature of the animals was taken twice daily. The result was negative. Experiments upon rabbits, guinea-pigs, rats, mice, and other animals were also negative. Cornil and Babes injected pure cultures into the peritoneal cavity and into the duodenum of rabbits and guinea-pigs without success.

Fraenkel and Simmonds in a series of experiments upon different animals showed that pure cultures injected into mice and rabbits may cause the death of these animals, and that the bacilli may again be obtained in pure culture from their organs. Although the symptoms produced in these animals were not those of typhoid fever, yet the fact that death was caused by the introduction of the bacilli was held to prove that the bacilli are pathogenic. In these experiments pure cultures of typhoid bacilli were injected into the peritoneal cavity in thirty-five mice, with a fatal result in twenty-seven cases. The results of these inoculations appeared to be influenced to a considerable extent by the amount and the concentration of the culture injected. In a number of the cases a dilute mixture failed to cause death, while a concentrated mixture, injected into the same animals later, succeeded. These facts suggest the question, whether the fatal results may not have been caused, not by the bacilli themselves, but by certain toxins developed by their growth in the cultures.

Seventy-nine rabbits also were treated in different ways. Pure cultures were injected into the intestine five times, into the subcutaneous connective tissue five times, and once into the lung. Inhalation of the bacilli was tried twice. All of these experiments failed. Injections into the peritoneal cavity in twenty rabbits caused death in but two, and forty-six injections into a vein of the ear gave twenty fatal results. In the fatal cases the bacilli were obtained from the spleen by culture and they were also demonstrated microscopically in sections. The arrangement of the bacilli in groups was precisely the same as that seen in the spleen in cases of typhoid fever in man. The fact that the comparatively large amount (one-third to two syringefuls) of pure culture used in these experiments caused death, after an interval of a few hours up to two or three days, in only twenty-two out of seventy-nine cases indicates that the typhoid bacillus is only moderately pathogenic in rabbits. It is nevertheless to be borne in mind that differences in lesions and symptoms produced by a certain bac-

terium in man and animals do not prove that the bacterium in question is not pathogenic in such animals. In support of this statement Koch cites the different manifestations of disease in man and in animals produced by the anthrax and tubercle bacilli. Germano and Maurea succeeded generally in causing death in mice in from one to three days by means of an intraperitoneal injection of 0.1 c.c. of bouillon culture two days old. The pathological findings were similar to those in mice killed by the colon bacilli. The more quickly the animal died, the more numerous were the bacilli found in its body, as a rule collected into the characteristic little groups within the organs. In slower cases the bacilli could also be found both by culture and in sections, but in much smaller numbers. Proliferation of the bacilli unquestionably took place in the first case, while in the second the injected bacilli were disappearing; but death resulted from their toxic action. The same thing occurs in guinea-pigs, according to Lösener, when 0.003 gm. of an agar culture one day old is injected into the peritoneal cavity, and of dogs and rabbits when intravenous inoculations are made with large doses. According to a number of experimenters, subcutaneous injections of sufficient strength, especially in dogs and rabbits, cause abscesses to develop which contain the typhoid bacillus in pure culture.

Fatal poisoning can also be caused by cultures sterilized by heat or by filtration, the process corresponding to that due to infection by living bacilli. Changes in the intestinal canal are the predominating feature in these cases, as is true also of animals infected by the colon bacilli. The lymphatic system of the mucous membrane, the mesenteric nodes, and the spleen are often specially affected. It is usual for the body temperature of the animals to rise for a short time and then to fall rapidly below the normal.

Brieger made some investigations in regard to the chemical substances which are produced by the growth of the typhoid bacillus in cultures. In a number of cases he succeeded in obtaining a deliquescent basic substance, always in very minute quantity. He considered this to be a ptomain. This substance caused death in guinea-pigs in from twenty-four to forty-eight hours. The typhoid toxins can best be demonstrated, according to Pfeiffer, by killing fresh agar streak cultures with chloroform vapor, or by heating to 54° C. for one hour, and using the dead bacteria for injection. Three to four milligrams represent the fatal dose for a guinea-pig weighing 100 gm. At the present time, little more is known of the nature of this toxin than the fact that it is more or less destroyed by high temperatures.

Chantemesse and Widal, by using freshly isolated cultures of typhoid bacilli, claimed to have caused not only the poisoning, but

also the infection of mice and guinea-pigs. Old cultures became virulent when injected subcutaneously in these animals if at the same time a considerable quantity of sterilized streptococcus bouillon was introduced into the peritoneal cavity. Cultures from these animals required less of the sterilized streptococcus bouillon to cause death in the second animal. After being passed in this way through a series of twenty-five animals the typhoid cultures became so virulent as to cause death without the aid of the streptococcus bouillon. The disease thus produced was septicæmic in character and had little resemblance to human typhoid. Sanarelli also increased the virulence of typhoid bacilli by sterilized cultures of colon bacilli and of the bacillus prodigiosus.

Lépine and Lyonnet injected pure cultures of typhoid bacilli into a portion of the intestine of a dog, confining them in this situation by means of ligatures for three days. No symptoms of disease were produced. When the animal was killed, on the twentieth day, no lesion of the mucous membrane of the intestine was found, nor was the spleen increased in size. The mesenteric lymph nodes, however, were greatly swollen. The infection was general and of the nature of a septicæmia. The blood serum in strength of 1:100 produced the characteristic reaction of Widal.

It is a more difficult matter to infect or poison animals by the mouth. The experiments of the earlier writers were not successful, and the later ones have given few successful results and these have not been uniform. The same is true of inoculations in the intestinal canal. Infection by inhalation also has rarely succeeded (Cygnæus).

The immunization experiments of Pfeiffer and others have demonstrated that the typhoid bacillus produces a specific effect in animals comparable to that in human beings, although differing in lesions and symptoms. Animals immunized in the usual way, by repeated small and increasing doses of typhoid bacilli, are proof against these bacilli and their toxins, even in large doses. At the same time they are as susceptible as before to the action of the different members of the colon group. The blood serum of the immunized animals protects other animals against the typhoid bacilli and their toxins, but not against the colon bacilli. The reverse of this also is true. These results have been fully demonstrated by different experimenters and are constant. This may be considered the final proof both of the identity of the typhoid bacillus and of its specific nature.

From the work done on animals we may conclude that typhoid bacilli are capable of proliferating in the bodies of living animals only when taken in large doses, and then only to a limited degree; also, that the animals are killed by a toxin produced by the bacilli, and

which acts chiefly on the intestinal canal. The lesions in animals which resemble those due to the typhoid process in man are seen also as a result of infection by the members of the colon group. Typhoid fever as seen in man has not yet been reproduced satisfactorily in animals.

The Transmission of the Typhoid Bacillus.

The bacilli escape from the body for the most part in the fæces and urine. Since the methods of separating the typhoid bacillus from other bacteria have been improved they have been demonstrated in the fæces in about fifty per cent. of the cases examined. Richardson found them in ten out of thirteen patients, in nineteen out of fifty-five specimens. Some observations tend to show that typhoid bacilli may be present in the fæces of people not suffering from typhoid fever. Remlinger and Schneider claimed to have found them in fifty per cent. of non-typhoid cases. One other such case has been reported in an attendant upon typhoid patients. Richardson examined the fæces of non-typhoid patients during life seventeen times and post mortem twelve times, and was never able to find any typhoid bacilli in them. Cases which will be referred to later show that these bacilli may remain in the gall-bladder for long periods of time. They may, therefore, perhaps escape into the alimentary canal, and be discharged from the body when there is no manifestation of fever. The urine has also been found to contain bacilli for weeks and even months after recovery. They are said to become more abundant in the fæces when the stage of sloughing in Peyer's patches arrives. They are sometimes found as early as the seventh day, and usually disappear soon after convalescence has set in. They have been seen forty days after the temperature had become normal. Richardson found typhoid bacilli in the urine in nine out of thirty-eight typhoid patients, in forty-four out of one hundred and seventy-two specimens. When found, they were in large numbers and in nearly pure culture. They appeared first in the later stages of the attack, generally persisting far into convalescence; in two cases they were found ten days after the patients had been discharged from the hospital. They were nearly always associated with albuminuria and casts. The bacilli also escape to some extent in the expectoration, for they have been found in the sputum and in the mucous membrane of the larynx, which is quite liable to typhoid ulcerations. They have also been found in the sweat.

It has been already shown how resistant these bacteria are in the face of many conditions which we would naturally have supposed to be very unfavorable. It is possible, therefore, that they may live

after their discharge from the body for months in various places and conditions, as if waiting to be picked up and conveyed in some way to new victims. They are rarely conveyed directly from the sick to the well, although this does occasionally occur.

Typhoid fever is not actively contagious, in the sense in which scarlet fever and measles are, that is, there is no danger in being simply in the immediate presence of a typhoid patient. Other patients in the same wards with sufferers from typhoid almost never contract the disease from them. Attendants do, however, a little more frequently, and this is undoubtedly due in most instances to their handling the clothing, the bed linen, and the utensils of various kinds which have come in contact with the patient, and have been soiled by his discharges. Yet even such cases are rare. I have had occasion to treat a few attendants who were taken down while caring for cases of typhoid fever, or within a fortnight thereafter. But Osler states that during six years, only one nurse, one orderly, and one patient contracted the disease in his wards. Clothing and bed linen which have been soiled by the patient, and utensils such as urinals and syringes, may convey the disease to others, not in immediate attendance. Murchison relates an interesting case in which the poison was apparently carried on soiled linen from one patient to another. The committee of the Clinical Society concluded that typhoid infection may be conveyed by fomites and may be retained in them probably for two months at least. It is natural to suppose that insects, such as flies, may carry the germs from the discharges, and directly infect others, or deposit the poison upon food. Simmonds, Craig, Burgess, Hoffmann, Veeder, Sangree, and others have shown that microorganisms may be conveyed by flies. Many of the instances in which a number of people living in the same house are attacked by typhoid fever are, of course, explained by a common origin of the poison, but among them there are some instances more easily explained as due to a direct conveyance of the poison from the sick to the well.

The transmission through the air either directly from the patient or from decomposing refuse, as by sewer gas or from old collections of dust, which was formerly considered to be an important mode of transmission of the poison, is now believed to be a rare occurrence. It has been shown that the dry bacilli may be suspended in the air. Some have thought that they found them in the dust of a building where there had been cases of typhoid fever. Some have thought that the gas escaping from open drains or air blowing over polluted soil has been an important factor in causing attacks of typhoid, but where these unfavorable conditions exist there are doubtless other ways than through the air by which the germs may have been spread.

The transmission of typhoid bacilli has been more frequently, clearly, and strikingly shown to occur by means of drinking-water than in any other way. A great many epidemics of typhoid fever have been thoroughly studied and carefully described which showed most strikingly the origin of this disease from the water supply. A few instances will be of interest. At Maidstone, in England, in 1898 an epidemic occurred in which nineteen hundred and eight cases of typhoid fever were reported, out of a population of thirty-five thousand. Different districts of the town were supplied with water from different sources; almost all of the cases occurred in those districts receiving their water from a single source. A number of cases, to be sure, occurred in that part of the town which did not receive water from this source; but this can be readily accounted for by the fact that the inhabitants of course did not remain always in the same district but visited in different parts of the town, and by the further fact that articles of food and other contaminated articles may have conveyed the disease from one district to another. The water which supplied the most severely affected portions of the town came in part from reservoirs so located as to be liable to contamination; one of them was very close to a gypsy camping ground, and also to a refuse heap where crowds of hop-pickers were wont to empty their bowels.

In 1885, in Plymouth, Pa., twelve hundred people were attacked with typhoid fever. The cases began to appear about the 10th of April at the rate of fifty a day. Most of them were in a part of the town receiving water from a certain stream. During January, February, and March there was a man ill with typhoid fever in a cottage about seventy feet from this stream. His attendants were in the habit of throwing the evacuations on the ground towards the stream. During these months the ground was frozen and covered with snow. In the latter part of March and early in April there was a heavy fall of rain and a thaw, and at the time of this thaw the patient had numerous copious discharges; these and much material from the earlier evacuations must have been washed into the stream.

Ernest Hart has collected and analyzed two hundred and five epidemics in Great Britain showing their dependence upon pollution of the water supply. This pollution may occur in various ways—by the proximity of wells or reservoirs to drains, sewers, cesspools, privies, deposits of refuse, graveyards, etc. If drains or sewers are leaky or otherwise defective, or if they overflow, the danger of contaminating the water supply is of course increased. Brooks or reservoirs may be polluted by the carelessness of tramps, workingmen, or others suffering from typhoid fever, but still able to be about. It has been

noticed that following severe rain storms there is sometimes an increase in the number of cases of typhoid fever. This is probably due in many instances at least to the washing of contaminated discharges into streams or reservoirs from which water is supplied. Hart concludes from his studies that in some instances a long interval of time elapses in many of these cases of water-borne epidemics between the deposit of infected material in some dangerous place and the outbreak of the epidemic through the water supply. (See also Volume XIII., pp. 302 *et seq.*, of this series.)

In other striking instances the milk supply has proved to be the origin of a typhoid epidemic. One very remarkable instance of this kind, occurring at Clifton, Bristol, England, was studied and described by Dr. Davies, medical officer of health of the city of Bristol. The location of the cases having indicated that the origin of the epidemic lay in milk coming from one place, a search was made for the source of contamination of that milk. For a long time no explanation appeared, but it was finally learned that a man working in the fields, on the side of the valley from which this milk was brought, had not been well, though continuing at work. He had had frequent evacuations from his bowels in the fields, and, when found by Dr. Davies, his blood gave a good Widal reaction. Water from the stream running through this valley was used to wash the cans which conveyed the milk.

In 1895 an epidemic of typhoid fever, occurring at Stamford, Conn., was clearly traced to a certain milk supply. Of the four hundred and six cases occurring at that time, three hundred and fifty-five were in families which received their milk from a single dealer. The sale of this milk was stopped by the authorities, and within two weeks there was an almost complete cessation of new cases. A well connected with the dairy from which this milk came was within twenty-five feet of a privy, and the natural surface drainage was towards the well. This privy had a shallow vault which was leaking at the surface. The door was not kept locked, and was therefore accessible to tramps. The water in the well was examined and found to contain such elements of contamination as might come from privies.

Oysters have been very clearly shown, in some cases, to be the agents conveying the germs. Dr. Conn, of Middletown, Conn., investigated a small epidemic at Wesleyan University in 1894. There were twenty-three cases of typhoid fever among the students. All but three of the cases were in members of three out of seven college fraternities. Twenty-five per cent. of the members of these fraternities suffered from typhoid fever. Only one article of food or drink was used by students belonging to these three fraternities and not

used equally by members of the other four; this article was oysters, and they were eaten raw. Six visitors to the banquets at which these were eaten also developed typhoid fever. The oysters came from a creek within three hundred feet of the outlet of a sewer, where they had been fattened by being kept in the brackish water, and at this time there were two persons in the incubation period of typhoid fever in the house supplying the sewer. The use of oysters from the same locality by students at Amherst College was followed by an outbreak of typhoid fever among those who ate them. Chantemesse also, in 1896, reported a small outbreak of typhoid due to oysters. It was in a village where there had been no case of typhoid fever for about a year. A merchant there imported a lot of oysters which were eaten raw by fourteen people. All of these were taken sick, while none of those living in the houses where the oysters were consumed, but not partaking of them, were affected. Eight of these fourteen patients had slight gastrointestinal attacks; four others were ill for about three weeks with prostration, abdominal pain, tympanites, tenderness, and dysenteric movements; the remaining two had severe attacks of typhoid fever. Foote, of New Haven, has shown that typhoid bacilli with which oysters have been intentionally infected may be found in them even after thirty days from the date of infection. Even in extremely cold weather they may live in unsterilized salt water or brackish water for at least eight days. In warm water they rapidly diminish in number after the first week, and cannot be detected in the water after three weeks. He also showed that the typhoid bacillus lives longer in the juice and stomach of the oyster than it does in the water in which the oyster grows. Chantemesse found that oysters placed in sea water intentionally contaminated by typhoid cultures, and removed at the end of twenty-four hours, still contained after that time both colon bacilli and typhoid bacilli.

Other articles of food may be accidentally infected. Careless and uncleanly individuals, domestic animals, or insects may convey the infectious material, or the receptacles holding them may have been washed with contaminated water. Ice-cream has sometimes appeared to be the cause of an outbreak. An epidemic occurring in Mid-Renfrewshire in 1893 was evidently due, at least in part, to the use of ice-cream sold by a dealer whose daughter was sick with typhoid but continued to work in the shop during most of her illness. Some epidemics have been attributed to the use of meat from diseased calves. Typhoid fever, however, has never been recognized in animals, and it is difficult to avoid the suspicion that there may have been some other source for these epidemics.

PATHOLOGY.

For one or two weeks usually after the bacillus of typhoid, the Eberth bacillus, has by chance found lodgment in an individual, no effects, or but very slight ones, are produced. In some cases—we have seen that we do not yet know in how many—these bacilli may remain alive in one or another portion of the body for long periods of time with little or no effect. Usually, however, in one or two weeks after the introduction of the bacilli decided effects begin gradually to show themselves. These bacilli have been found in nearly every organ and tissue and fluid of the body in which they have been looked for, they escape with the urine and the fæces, and may also make their way through the placenta into the fœtus.

Lodging in these various parts and scattering everywhere their poisonous products, they produce many abnormal effects.

These effects may be put into two groups—intoxication and anatomical lesions. In the majority of ordinary cases of typhoid fever the toxic effects decidedly predominate; the local lesions and the symptoms depending directly upon these lesions play in most cases a less conspicuous part. Among the prominent toxic effects of the disease are the elevation of temperature, characteristic in its duration and its variations, the prostration, the general pains, and the disturbances of the nervous system. The disturbance of the circulation, and probably also the distention of the abdomen, are in part effects of the intoxication.

But the typhoid bacilli and their products not only interfere with the functions of the organs by their poisonous action, but even cause structural changes in them. The tissues are excited to rather characteristic histological alterations. The smaller lymph channels, more particularly in and around nodules of lymphoid tissue, are especially sensitive to the infection, and react principally in the way of cellular proliferation. This, with some congestion and inflammatory exudation, produces a marked swelling of the lymph organs, and frequently ends in such an obstruction to the local circulation that necrosis results, and a sloughing of exposed surfaces. In other cases or in other parts of the same patient the bacilli may have a true pyogenic power, causing suppurative inflammation in various organs and tissues. Degenerations of various kinds are also commonly produced in different organs, as is the case in many infectious diseases, especially in the protoplasm of the cell bodies.

The bacteria of this disease seem to have an especial fondness for certain parts of the body. These parts are the lymphoid structures

of the lower end of the ileum, the mesenteric lymph nodes, and the spleen, and then the mucous membranes of the rest of the ileum, the large intestine, the jejunum, the larynx, the pharynx, and the gall-bladder, and the bones. The blood-vessels and the liver seem to hold a position of less favor. The most noticeable lesions found in this disease are those of Peyer's patches. They become enlarged and congested, necrotic, ulcerated, and later cicatrized. The other mucous membranes above mentioned may show similar changes. The lymph nodes and the spleen become enlarged, and the bones and their periosteum may be inflamed. Some of the blood-vessels are occluded by the proliferated endothelium or by clots caused by these cells as they break down, and these obstructions lead to necrosis, as seen in minute foci in the liver, ulcers of various size in the mucous membrane, and gangrene of exposed parts.

The debility and poor state of nutrition induced by all these results of the infection, aided by the pressure on certain parts, may cause bed-sores. These bed-sores, gangrenous areas, and ulcers, furnish a convenient means of entrance for the pyogenic cocci and other bacteria, and so lead to an additional infection by these germs—a mixed infection—adding the lesions and dangers of pyæmia.

The Anatomical Lesions in Detail.

The Intestines.

The most striking changes in this disease, and those which have formed the basis for its satisfactory recognition as a distinct morbid entity, are those of the lymphoid structures in the lower part of the small intestine. Peyer's patches and the solitary follicles of this region, in almost every case of typhoid infection, undergo characteristic changes, as was first fully demonstrated by Bretonneau. These changes have been of late thoroughly studied microscopically by Mallory, of Boston, who concludes that they consist chiefly of a marked proliferation of the endothelial cells, especially of the small lymph channels. This is most apt to occur in the sinuses—that is, in the more open parts of the lymph follicles—and in the immediate neighborhood of these follicles. Mallory found the proliferation also in many small blood-vessels and some larger ones, involving the lining cells of the vessels, but more particularly cells lying a little beneath the free surface. It also occurs diffusely through the intestinal mucous membrane. These endothelial cells become not only greatly increased in number, but also greatly, sometimes enormously, increased in size, and exhibit a strong propensity to gorge themselves with lymph cells, sometimes with plasma cells, red blood cells, and polymorphonuclear

leucocytes. These huge infant cells are very apt soon to degenerate, and as they crumble seem to precipitate a coagulation of fibrin, that is, the formation of thrombi. This is apparently the chief factor in the obstruction of the vessels and the death of the tissues. This proliferation is accompanied by a proliferation of the lymph cells and the plasma cells and by some exudation of these cells from the blood-vessels. Polymorphonuclear leucocytes do not accumulate in any considerable numbers in these ordinary typhoid inflammations, but when secondary infection follows necrosis and when the typhoid germs show pyogenic powers, such leucocytes accumulate and emigrate from the blood-vessels, sometimes in great numbers.

The changes as they appear on gross examination may be divided into four stages: hyperæmia, "medullary infiltration," necrosis and ulceration, and cicatrization. These anatomical stages correspond fairly well to the stages observed clinically. The first stage, that of hyperæmia, corresponds with the beginning, sometimes with the whole, of the first week; but we rarely have an opportunity to see the intestine at this stage, and it is doubtful how constantly and how extensively this simple hyperæmia may occur. In some of those rare cases, when there has been an opportunity to examine the intestinal mucous membrane in the first week of an attack, it has been observed that there was a distinct hyperæmia of the mucous membrane of the lower part of the ileum and the beginning of the large intestine. It has been suggested that perhaps in some cases of abortive typhoid there may be no further lesions, and on the other hand, that in certain forms of the disease a diffuse catarrhal swelling may reach a high grade. In the beginning of the second week, in the severe cases even at the end of the first, the medullary infiltration reaches its height, and it is apparently the rule that at this time the diffuse hyperæmia and swelling of the mucous membrane diminish. The Peyer's patches seem to start before the solitary follicles in this process. We sometimes find an equal amount of change in the two kinds of structure, but it is not usual to find solitary follicles with more advanced changes than the Peyer's patches in the same intestine.

Naturally, the form and the situation of the typhoid lesions correspond in general with those of the lymphoid structures in which they occur. Those situated in the Peyer's patches are usually elongated, though somewhat rounded, their length being parallel with the axis of the intestine. They are usually found opposite the attachment of the mesentery, sharply outlined, flat, with borders overlapping a little. The color is at first deep red, then grayish-red, and, as the necrotic stage approaches, grayish-yellow. The patches may be elevated several millimetres, sometimes as much as eight. The sur-

face is sometimes velvety, but it may be granular or nodular. In some cases the consistence is quite soft, in which instance the patches have been called *plaques molles;* at times they show considerable induration, when they have been called *plaques dures.* This medullary swelling may extend beyond the original outlines of the patches. Several patches may run together, forming very long lesions parallel with the axis of the intestine. On the other hand, a patch need not be affected throughout its whole extent. The solitary follicles are infiltrated in varying degrees, and in varying distribution. They may reach the size of a pea or that of a cent. At times they are found in a more or less perfect chain encircling the intestine, and this may result later in a cicatricial stenosis.

In the second week, often at its commencement, the retrogressive changes begin. Some degree of necrosis has been seen as early as the fifth day, though it may be delayed until the end of the second week. These changes may advance in either of two directions: to resolution on the one hand, or, on the other and more commonly, to necrosis. Both kinds of change may be seen in the same case, even in the same patch. When resolution begins, a grayish-yellow color appears, then a depression at the centre, which spreads to the periphery. When necrosis begins, the spots assume a grayish-yellow color, then become dirty-gray, and afterwards dirty-green. These changes are not often uniform within the same Peyer's patch, and therefore the slough does not usually fall off in a single piece, but in separate particles of varying thickness. We may, accordingly, find patches where bits here and there have been lost, producing a very irregular appearance, reported by Louis under the name of *plaques gauffres.* In those patches which are deeply infiltrated and much indurated, the slough is more apt to come away entire; but this is not so frequent an occurrence. The resulting ulcerations vary greatly in area and in depth. All that has been said in regard to the size and shape of the infiltrated areas will apply to the ulcers. In depth, they sometimes hardly penetrate the mucous membrane, or on the other hand they may be so deep as to leave only a fine layer of the serosa, or may even include a part of that, so that when the slough falls away a perforation results. The edges are sharply defined, and at an early stage somewhat thickened. The floor may be very uneven. At first it is of a deep red color, later more grayish. After the ulcer has been formed it may become greatly deepened, resulting in perforation quite late in the process.

Hemorrhage is a frequent result of the ulceration. These hemorrhages may come from large vessels whose ends are easily seen, or from minute vessels which we cannot discover at autopsy. Those from large vessels seem to come particularly where the so-called *plaques*

dures have been thrown off in large masses, and are the most abundant and rapidly fatal hemorrhages. The hemorrhages from the minute vessels are often found in the earlier stages of necrosis, before a slough has been thrown off. The patches then may have a spongy, swollen, shaggy appearance. In such cases there may be frequent and abundant hemorrhages before the end of the second week.

Hemorrhages occur, according to Griesinger, in 31 per cent. of the fatal cases; Liebermeister, 39 per cent.; Homelle, 44 per cent.; Curschmann (in Leipsic), 38 per cent.; Curschmann (in Hamburg, 1886), 21 per cent.; Curschmann (in Hamburg, 1887), 12 per cent.

Cicatrization of the typhoid ulcer often takes more time than the preceding stages. The length of time depends upon the size of the ulcer and upon the general physical condition. When there is great physical prostration, the ulcers may be a long time in healing, and this has given rise to the term "atonic" as applied to the ulcers by the older writers. After cicatrization, the affected spots are depressed, thin, smooth, and at first pale; later they may become pigmented, especially at the edges. The occurrence of a previous attack of typhoid fever can often be asserted from the appearance of these spots at autopsy, months and perhaps years after. Some observers believe that these spots may be afterwards covered by villi.

The extent of these changes varies greatly in the different cases. The intensity of the infection, and the condition of the individual must, of course, have much to do in determining the extent, but beyond this general belief we have no explanation of the causes of difference, except as we find that age and sex are modifying influences. In children these changes, as a rule, are much less marked, and there is a greater tendency to resolution.

As has been stated, the very lowest part of the ileum is the portion of the alimentary canal most frequently and most intensely affected, and the farther one goes from this region the less the frequency and intensity of the changes, though the pharynx and adjacent cavities, and also the gall-bladder, show a greater tendency to ulcers than the stomach or duodenum.

In some cases only one spot of ulceration may be found; in others hardly any patch escapes in the lower two-thirds of the ileum, and the enteric mucous membrane near the ileocæcal valve may be changed into an ulcerating surface. Curschmann found in one case thirty-six diseased patches; others have reported even larger numbers. A moderate number of ulcers is, however, much more common.

Curschmann's statistics from Hamburg and Leipsic of 577 autopsies show the ileum affected in 510 (88 per cent.); the cæcum, some-

times involving the appendix, in 247 (43 per cent.); the colon in 184 (32 per cent.); the jejunum in 41 (7 per cent.); and the rectum in 12 (2 per cent.).

Hoffmann, in an epidemic at Basle, found the large intestine involved in 40 per cent., Griesinger, of Zurich, in 40 per cent., while in Tübingen it was involved in only 24 per cent. The most frequent combination of sites is ileum, ileocæcal valve, and cæcum; the beginning of the colon is often involved with the cæcum. Less frequently we find the ileum alone or the ileum and lower half of the jejunum; still less frequently the cæcum and colon alone or only the lower part of the large intestine. And cases have been reported in which the only ulceration was in the vermiform appendix. In the upper part of the jejunum and the duodenum most authors have failed to find a specific ulceration. It is, however, said that Hamernik reports such an observation.

Typhoid Fever without Intestinal Ulceration.—The great diversity in the amount of change in the intestines in different cases, and the fact that those changes are sometimes extremely slight, suggest the possibility that they might be absent occasionally in people infected by the typhoid bacilli. Moreover, many cases have been reported which clinically presented a picture of typhoid fever, but in which the autopsies failed to reveal the presence of changes in Peyer's patches.

Louis, though stating that we must consider this lesion not only as peculiar to the typhoid affection, but as forming its anatomical character, just as tubercles form that of phthisis, has nevertheless cited an observation in which the complete group of symptoms was observed during life, but in which the autopsy did not reveal any traces of lesion in the intestinal lymphatic apparatus.

Before we became familiar with the distinguishing features of the typhoid bacilli, there was usually some degree of doubt as to the diagnosis of those cases. But recent bacteriological investigations have tended to confirm the view that intestinal ulceration, though usually present, is not invariably so, in cases of typhoid fever.

Passing over a considerable number of cases in which the clinical diagnosis was not confirmed by bacteriological investigation, we come to some recent cases in which the presence of the typhoid bacilli has been demonstrated, though the characteristic lesions of the small intestine were wanting. Du Cazal, in 1893, recorded a carefully observed case of a youth, aged nineteen, who died of an attack of typhoid fever on the thirteenth day, in which at the autopsy there were found a double pneumonia, swelling of the spleen and mesenteric lymph nodes, but absolutely no change in the appearance of the

mucous membrane of the small or large intestine. A microorganism was cultivated from the spleen in pure culture, which in the biological characters observed appeared identical with the Bacillus typhosus.

Cheadle (1897) reports the case of a boy, aged three, whose brother and sister were for some time in the hospital suffering from typhoid fever; he had diarrhœa, vomiting, and prostration, was apathetic, showed three rose-spots on the abdomen and four or five on the back, which faded on pressure. The abdomen was tympanitic and the liver was enlarged, but the spleen was apparently not enlarged. The boy had been previously healthy. On the twenty-first day a Widal reaction was obtained. On the twenty-sixth day typhoid bacilli were separated from the urine by Parietti's method. On the thirty-second day a Widal reaction was again obtained. He died on the thirty-third day. At the autopsy no ulceration of the intestines was visible. Cultures from the spleen showed typical colonies of the typhoid bacillus. Mesenteric glands and liver were enlarged. A Widal reaction was obtained from the blood of the right auricle.

Guinon and Meunier, in 1897, reported a case with the clinical features of pulmonary tuberculosis and typhoid fever—the physical signs of pulmonary tuberculosis, enlargement of the spleen and liver, rose spots on the abdomen, and a good Widal reaction on two occasions. The patient died on the thirtieth day. In the ileum there were small ulcers, apparently tuberculous to the naked eye, and under the microscope showing the histological changes of tuberculosis, also tubercle bacilli. Cultures from the spleen, pleura, and lung showed bacilli which gave all the characteristics of typhoid bacilli, including a good Widal reaction with serum from two typhoid cases.

Many other cases have been reported in which typhoid bacilli were identified without the characteristic typhoid lesions in the intestines, and some without any lesions of the intestine and with other clinical pictures than that of typhoid fever.

Guameri, in 1892, relates an interesting case of typhoid infection of the bile vessels, without typhoid changes in the intestines. Bacilli cultivated from the liver and spleen, and also from the blood twelve days before death, gave all the biological characteristics of the typhoid bacillus. Another observer reports a case of acute febrile disease of the gall-bladder, which was opened and found to contain, besides calculi, also the typhoid bacilli. The blood gave a characteristic Widal reaction.

We find mentioned a case of death from purulent pleurisy. None of the intestinal lesions of typhoid was found, but in the pleural fluid there were typhoid bacilli. In another case of fever the patient died on the tenth day, five days after the onset of symptoms of meningitis.

No lesion was found in the intestine, but in the fluid infiltrating the brain typhoid bacilli were obtained in pure culture. In still another case of suppurative meningitis following a fall, no lesions of typhoid fever were found in the intestines, but from the inflamed meninges were obtained pure cultures of typhoid bacilli. In a case of hæmaturia and coma, in which death occurred on the sixth day, the spleen and mesenteric glands were found enlarged, but the intestines were healthy. From the spleen typhoid bacilli were obtained. In a case of suppuration in an old goitre, typhoid bacilli were obtained from the pus, but there were no other evidences of typhoid infection.

Allowing for errors in some of the bacterial studies, these cases, taken in connection with those more numerous cases in which a clinical diagnosis has not been sustained by bacteriological investigation, leave little room for doubt that infection by the typhoid bacilli may occur without ulceration of Peyer's patches, and even without any intestinal lesion.

Perforation.—When the ulcer is so deep that the floor is very thin, the intestinal pressure in many cases cannot be resisted, and a perforation occurs. The unnaturally friable condition of the tissues, as the result of the inflammation, also tends to the production of this unfortunate event. A too great abundance or too firm a character of the intestinal contents will increase the danger of perforation; also excitement of peristalsis by improper food, straining to empty the bowels or bladder, or other exertions. If the perforation be due to the simple casting off of the slough, it is said to be punctate or rounded, but if caused by the intestinal pressure, it is often of a more linear shape or dentate.

Perforations occur especially in cases which have been running a severe course, but they have no special relation to the severity of the diarrhœa. They may be of any size, up to that of a twenty-five-cent piece. There may be several of them. Hoffmann records a case with twenty-five perforations; Curschmann a case with fifteen. The intestine sometimes presents a sieve-like appearance from the presence of several minute openings in one patch. They occur most frequently in those parts of the intestine where the changes in Peyer's patches and the solitary follicles are most likely to take place. Hoffmann describes a perforation in the jejunum. It may occur in various parts of the colon, in the sigmoid flexure, and even in the rectum. It is to be borne in mind that it may occur also in the vermiform appendix, and cases of typhoid fever have been recorded in which the only ulceration was in the vermiform appendix. We see, therefore, that there may be cases in which it is very difficult to recognize an appendicitis, even after autopsy or operation, as a typhoid affection, unless we make use of

the help afforded by bacterial examination. The site of the perforation was found in 167 cases, tabulated by Fitz, in the ileum, in 136 cases—81.4 per cent.; in the large intestine, in 20 cases—12.9 per cent.; in the vermiform appendix, in 5 cases; in Meckel's diverticulum, in 4 cases; in the jejunum, in 2 cases.

In 64 perforations investigated by Curschmann, there were found to be in the upper part of the ileum, 5; in the lower part of the ileum, 39; in the region of the valve, 7; in the vermiform appendix, 1; in the colon, 11; in the rectum, 1.

Perforation most commonly occurs at that time in the course of the disease when we know that the slough is most apt to be thrown off. The time at which it may occur is seen by this table from Fitz:

First week	4 cases.	
Second week	32 "	16.5 per cent.
Third week	48 "	24.8 "
Fourth week	42 "	21.7 "
Fifth week	27 "	14 "
Sixth week	21 "	13.4 "
Seventh week	5 "	
Eighth week	3 "	
Ninth week	2 "	
Tenth week	4 "	
Eleventh week	3 "	
Twelfth week	1 "	
Sixteenth week	1 "	
	193	

In 73 cases Curschmann found it to occur from the eleventh to the twentieth day, 23 times; twenty-first to thirtieth day, 31 times; thirty-first to fortieth day, 13 times; after the fortieth day, 6 times. He has seen it occur after the fiftieth or sixtieth day, and once even after the one hundredth. It is less frequent in children than in adults; in women than in men. It is rather more frequent in the poorer classes.

Fitz gives the following figures of its occurrence at different ages: From one to ten years, 3.6 per cent.; ten to twenty, 23.8 per cent.; twenty to thirty, 39.8 per cent.; thirty to forty, 23.3 per cent.; forty to fifty, 7.2 per cent.; fifty to sixty, 1 per cent.; sixty to seventy, 0.5 per cent.

The frequency with which it is found at autopsy has been variously observed by different investigators. Murchison found it in 21 per cent. of autopsies, Herschel in 4 per cent., Brouardel and Thoinot in 11 per cent., Griesinger in 12 per cent., Curschmann in 10 per cent., Hoffmann in 8 per cent. It is less frequent than hemorrhage, and is thought not to occur in over 3 per cent. of all cases; according to

Griesinger's statistics, in 2.3 per cent.; Curschmann's Leipsic statistics, in 2.2 per cent.; Curschmann's Hamburg statistics, in 1.6 per cent. It appears to vary in frequency in different epidemics.

Perforation is followed by *peritonitis.* In a few cases, the situation or the size of the perforation may be such that a very minute amount of the intestinal contents escapes, and temporary adhesions limit the spreading of the infectious material. Later these adhesions may give way, perhaps to be followed by others with wider limits, producing an alternation of advances and remissions in the symptoms. In other cases, the shock may be so intense that death follows before time has elapsed sufficient for the development of any peritonitis which can be recognized by the naked eye. While the peritonitis which follows the perforation is usually general, adhesions may encapsulate the escaped intestinal contents and the inflammatory products, forming local peritoneal abscesses, either without or in addition to a general peritonitis. The iliac fossæ, the pelvis, and the neighborhood of the liver are the places of choice for such localizations.

Peritonitis in typhoid is not always due to perforation. It may follow extension of inflammation from the ulcers through the thin remaining wall. It may also be due to rupture of the spleen or of the mesenteric glands, when these organs are the seat of softening or abscess, to rupture of the gall-bladder, of the bile ducts, or of a liver abscess. It has been found secondary to thrombosis of the intestinal vessels and gangrene of the intestine. A general peritonitis following perforation probably never heals spontaneously.

Mucous Membranes Other Than Intestina

The tendency which typhoid bacilli show to produce changes the lymphoid structures of the mucous membrane is not limited to the intestines. It appears rarely in the œsophagus, and very rarely in the stomach. More commonly than in either of these two situations, it is found in the pharynx and larynx, especially the latter.

The Larynx.—Catarrhal appearances in the mucous membrane of the larynx are rather common occurrences. They are frequently quite extensive, though rarely serious, but there are more severe changes in the larynx which are of greater interest and importance. Luening has collected 200 cases of typhoid disease of the larynx, and concludes that it is present in one-tenth of all autopsies. Hoffmann found laryngeal ulcers in 28 out of 250 autopsies. Griesinger found 37 extensive ulcers of the larynx in 349 autopsies. Some of these, especially those of the posterior wall, start from superficial erosions and fissures of the mucous membrane, which, from secondary infection,

become more extended; but some depend upon an infiltration of the lymph follicles, comparable in character with those seen so often in the intestines. They break down, like the other lymphoid infiltrations, and may lead to extensive ulceration, with perichondritis and destruction of cartilage. Many cases have been reported of extensive necrosis of the larynx. Death may be caused by œdema of the glottis, but a majority of the laryngeal ulcers remain superficial and small, and heal without leaving any traces.

The site of serious lesions of the larynx is given by Keen as supraglottic in 50 cases, infraglottic in 36 cases, glottic in 18 cases. The cartilages involved are given by Keen as cricoids, 43; arytenoids, 33; other cartilages, 7; by Lüning: Cricoid alone, 22; cricoid and arytenoids, 14; arytenoids alone, 9; cricoid, arytenoids, and thyroid, 3; cricoid and thyroid, 5; thyroid alone, 2.

A common site of the ulcer is the posterior inner surface from which it may spread, though as a rule only in the form of superficial erosions, to the posterior portion of the vocal cords. The ulcers are frequently found on the epiglottis. They are usually superficial. They may be solitary or in groups, running along the edge of the epiglottis. They may, however, invade the cartilage and destroy portions of its edge. Extensive destruction of the epiglottis is rare, but may involve more than half of it. It is maintained that laryngeal perichondritis may occur independently of ulceration of the mucous membrane. In such cases, the process must be compared with that of typhoid periostosis of the long bones and the ribs.

Typhoid bacilli have been found in the mucous membrane of the larynx. The ulcers belong, in general, to the height and the later stages of the attack—the time when in the intestine the throwing-off of the slough occurs and the cicatrization of the ulcers is accomplished.

Keen has found these lesions of the larynx to occur in the first week, in 7 cases; second week, 23 cases; third week, 30 cases; fourth week to two months, 83 cases.

Ulcers of the *pharynx* were spoken of as long ago as in the days of Louis and Jenner. They are usually superficial. The *nasal* passages sometimes show, in addition to catarrh, some superficial erosions.

The Ears.—Catarrhal processes of the pharynx may extend to the ear, the Eustachian tube and the tympanic cavity being frequently affected. The inflammation may be catarrhal, suppurative, or diphtheritic. Otitis media was found by Hengst in 28 out of 1,228 cases. Bezold found a disturbance of hearing in 50 out of 1,243 cases. Buerkner attributed 1.8 per cent. of all cases of deafness to typhoid fever; Zaufal, 0.7 per cent.; Kramer, 2.5 per cent.

Aural complications occur most commonly in the second or fourth week. The bacteria causing the trouble are generally pyogenic, but in a few cases the typhoid bacillus has been found. Suppurative inflammation of the middle ear may go on to perforation of the tympanic membrane or to suppuration of the neighboring structures, such as the mastoid cells and the adjacent sinuses.

The stomach rarely shows any specific changes in typhoid, only some swelling and redness of the mucous membrane. But cases have been reported of hemorrhage from typhoid ulcer of the stomach. Fenwick reports a case of death caused by severe hemorrhage from such an ulcer. In the *œsophagus* ulceration probably may occur, although it is very rare. One case of Osler's and one of Packard's, of Philadelphia, presented strictures of the œsophagus, probably resulting from cicatricial contraction of typhoid ulcers.

The Gall-Bladder.—Another mucous membrane which is very liable to ulcerative changes in typhoid fever is the gall-bladder. This is one of the favorite haunts of the typhoid bacillus. Gilbert and Girode found typhoid bacilli in the gall-bladder, and Chiari, in a series of observations, has shown that the typhoid bacillus as a rule is present here in cases of typhoid fever. He examined the organ in twenty-two consecutive autopsies on patients who had died of this disease, and was able to demonstrate it in twenty of these cases. Birch-Hirschfeld has had similar results. Richardson reports that a bacteriological examination of the contents of the gall-bladder was made in three autopsies of typhoid patients at the Massachusetts General Hospital, and that the specific bacilli were demonstrated in every case. Various observers have made cultures from the contents obtained during life on the occasion of surgical operations upon the gall-bladder, with the result that the typhoid bacilli were demonstrated in a number of cases, including some in which many months, or even years, had passed since the attack of typhoid. As Councilman has suggested, it is reasonable to suppose that the bacilli find their way to the gall-bladder through the liver. We know that they circulate with the blood, and the liver being commonly the seat of numerous small necrotic spots, there is an easy way of escape for the bacilli from the blood-vessels into the bile ducts. As we know that they can escape from the blood-vessels of the kidneys into the urine, it is easy to believe that they might more readily escape through these necrotic areas in the liver into the gall-bladder. These parasites are undoubtedly the principal cause of the ulcerations in the walls of the gall-bladder and the larger bile ducts, though other conditions, such as the presence of calculi, are undoubtedly contributing factors. It has been suggested that the typhoid bacilli may have some influence on the production of gall-

stones, but the facts already collected are not sufficient for us to form a conclusive opinion in regard to this. The gall-bladder perhaps forms a sort of base of operations from which the bacilli may from time to time make excursions and produce reinfection. The occurrence of ulcerative and diphtheritic inflammations of the wall of the gall-bladder and the larger bile passages has been noticed by various observers for a long time. They may result in abscesses of the liver or perforation with peritonitis, though such cases are rare.

The Mesenteric Lymph Nodes.

Next to the ulcers of the ileum, the first characteristic lesions to be noticed in typhoid fever were the changes in the mesenteric lymph nodes and the spleen. These are not the only lymphoid tissues besides those connected with the mucous membranes which the typhoid bacilli are likely to attack and alter, but they are the ones most prone to change. Those lymph nodes which correspond to the lymphoid tissues of the intestine usually selected by the typhoid bacilli for attack are themselves most sensitive to typhoid infection—that is, those corresponding to the lower part of the ileum and the ileocæcal valve. Those corresponding to the upper part of the small intestine and the lower part of the large intestine are quite commonly free or but slightly affected. There are, however, many exceptions to this rule. The retroperitoneal lymph nodes and those in the neighborhood of the stomach and the liver, as well as the bronchial nodes, are also frequently affected; sometimes those of the neck and the inguinal region. The changes in these structures begin at about the same time with the infiltration of the intestinal lymphoid tissues. In the beginning of the second week they are distinctly swollen, and the maximum of this change corresponds as a rule with the height of the disease; they may become enlarged to any size up to that of a hen's egg. We find them rounded, smooth or somewhat nodular, firmly elastic, and of a color from grayish-red to bluish-red. When such a gland is cut, the tissue bulges and the central part is of a grayer tinge than the outer part, or sometimes has a yellowish color. The retrogressive changes, also, keep step with those in the intestine, the size diminishes, the color becomes more pale, and they commonly assume their normal condition by resolution. They may, however, become softened, usually in small spots, of which there may be several in a single gland. This softened tissue may be absorbed; sometimes it is gradually replaced by calcified nodules, but it may end in a breaking down with perforation and peritonitis.

The Spleen.

The spleen is one of the organs in which the typhoid bacilli are most constantly and most abundantly found, and as a result it is commonly changed anatomically. In no other infectious disease, except malarial and septic troubles, is enlargement of the spleen so prominent as in typhoid fever; it occurs early in the attack, continues for a considerable time, and reappears quite regularly in exacerbations and relapses. In 300 consecutive autopsies reported by Curschmann it was enlarged in every case; there was a very large tumor 127 times, a moderate tumor 173 times; in 211 autopsies at Leipsic, also reported by Curschmann, there was a very large tumor 45 times, a moderate tumor 115 times, a small tumor 21 times, no enlargement 30 times.

Moderate enlargement is more common than great enlargement; the nodes are usually from two to two and one-half times the normal size, but they may reach six times the normal. As a rule the enlargement is greatest at the height of the disease; in the later stages of convalescence it cannot often be made out. Late in life the enlargement is less constantly present. Other conditions which may to a greater or less extent interfere with the swelling of the spleen are emaciation resulting from preceding disease and preëxisting local lesions of the organ, such as infarcts, chronic diffuse increase of the connective tissue, and inflammatory thickening of the capsule. In second and third attacks it is often absent. A swollen spleen may become somewhat diminished in size as an effect of severe hemorrhages, and sometimes probably of severe diarrhœa. In five hundred and seventy-seven autopsies reported by Curschmann, after subtracting those cases which seem to be explained by one of the above conditions, there remained only nine —that is, 1.6 per cent.—in which the enlargement was wanting, and there was no demonstrable reason why it should be so. There seems to be no correspondence between the enlargement of the spleen and the clinical type of the disease, as regards either the time when the enlargement appears or the degree which it reaches. An ordinary increase in size is seen in cases almost without fever. After the enlargement has made its appearance in an attack of typhoid fever, however, its failure to disappear may be considered a reliable sign that the attack is not yet ended, even though the temperature has become normal. In some cases the enlargement appears very early in the attack. Curschmann reports two cases in which it was noticed first during the period of incubation, three days and two days before the rise of temperature.

From the middle of the first to the middle of the second week the

organ is tense, smooth, and of a dark red color on section, unusually full of blood, and with indistinct markings; at the end of the second and in the third week it is still larger and softer, the pulp almost like gruel, of a very dark red, sometimes of a black-brown color. As the fever falls the volume diminishes quite rapidly, the capsule becomes relaxed, wrinkled, and the congestion disappears, while the hyperplasia, especially the stroma, continues. As a consequence the color becomes lighter, of a yellowish-red or a yellowish-brown, the markings of the stroma are more distinct, and the tissue is more tough. Mallory has found the same histological changes here as in the intestines, the proliferated endothelial cells showing a greater fondness for red blood cells, a large number of the latter being sometimes found in a single large cell. Other changes occasionally occur in the spleen. Among these are infarctions and abscesses. The infarctions may become softened, and the abscesses may result from these softened infarcts or may be merely a part of the general sepsis. These softened spots, whether they be results of infarction or abscesses, may break through the capsule and produce a general or a local peritonitis. It is said that a spontaneous rupture of the spleen may occur as a result of the enlargement and softening. In 577 autopsies Curschmann found infarction and hemorrhage 25 times, abscesses 4 times, rupture 2 times, extensive perisplenitis 16 times.

Griesinger's figures correspond pretty closely to these.

The Blood.

The typhoid bacilli have been found by culture in the blood by various observers, but as a rule they are found in only a few of the severe cases. Missul reports that he found them in each of nine cases examined. Kühnau, using from 5 to 10 c.c. of blood for each culture, found the organism in ten out of forty-one cases. Almquist and Silvestrini found them only occasionally. Bloch obtained them in one out of seven cases. Fraenkel, Simmonds, Lugatello, Seitz, and Gaffky failed in their attempts to isolate them from the blood. According to Cabot, with the exception of Kühnau, other observers have been successful in only seven cases out of one hundred and seventy-six cases examined. Neuhaus and Ruetmeyer claim to have found the bacilli in blood obtained by puncturing the rose spots, Neuhaus in nine cases out of fifteen; but Fraenkel, Simmonds, Seitz, Lugatello, Gaffky, Janowski, and Curschmann obtained negative results. From blood taken during life from the spleen, Chantemesse and Widal and many others have succeeded in obtaining growths of the bacilli, though some other investigators have failed. The bacilli have been found in

large numbers in the contents of the thoracic duct, giving rise to the suggestion that this is the principal channel by which they find their way from the intestines into the blood. Having once entered the blood, however, they are carried to the various organs and tissues of the body, and escape into the urine through the kidneys, and into the lumen of the intestine by the breaking down of the lymphoid structures in its wall. Pyogenic cocci are occasionally found in the blood, especially in the latter part of the disease.

The red cells of the blood diminish gradually in number during the course of the fever, and may show the changes commonly found in secondary anæmias; the hæmoglobin falls at the same time, but to a greater extent, and reaches the normal more slowly. The degree of anæmia is in general proportional to the severity of the case and may reach a dangerous point.

The most striking feature of the blood is the absence of any increase in the number of leucocytes. Exceptions are extremely rare save in the case of complications, and the number is often considerably diminished. In four hundred and ninety-four cases examined by Thayer the average of the counts was as follows:

Between	1,000 and	2,000	7	cases.
"	2,000 "	3,000	33	"
"	3,000 "	4,000	59	"
"	4,000 "	5,000	108	"
"	5,000 "	6,000	82	"
"	6,000 "	7,000	72	"
"	7,000 "	8,000	47	"
"	8,000 "	9,000	37	"
"	9,000 "	10,000	29	"
"	10,000 "	11,000	10	"
Over	11,000		7	"

Arranged according to the weeks of the attack when the examinations were made, he obtained these averages:

First week	21	counts.	6,984
Second week	50	"	6,468
Third week	40	"	6,260
Fourth week	28	"	5,877
Fifth week	16	"	6,621
Sixth week	5	"	7,000

A count in four hundred and ninety-one cases at the Massachusetts General Hospital corroborated Thayer's conclusions in a general way. Various complications may raise the number of leucocytes. Cabot refers to the following cases: One in which a perforation raised the number from 8,300 to 24,000; another case of perforation in which the number at the time of perforation was 18,500; a case of phlebitis

in which the number was raised from 6,400 to 12,900, falling one week later to 10,100; another case of phlebitis in which the number rose from 4,800 to 6,200; a case of mastoid abscess in which the number rose from 5,300 to 16,400; a case of otitis media in which the number rose from 8,400 to 11,200; another case of otitis media in which the number rose from 7,200 to 14,000; a case of abscess of the buttock in which the number rose from 8,000 to 11,200; and a case of hemorrhage in which the number rose from 8,000 to 11,300. Cabot says that general bronchitis has usually no effect in augmenting the leucocyte count unless this disease invades the smallest tubes, and cystitis also had no effect in two cases, and he is of the opinion that the complications directly due to the Eberth bacillus, such as cystitis or pneumonia, do not raise the number of leucocytes. In case of great exhaustion a complication may fail to produce any leucocytosis, and, on the other hand, leucocytosis is occasionally seen where it is impossible to make out the presence of any complication. In such cases, however, as Cabot points out, the possibility of a secondary infection, an osteomyelitis or a phlebitis of internal veins cannot be positively excluded. The polymorphonuclear leucocytes gradually diminish and the lymphocytes increase in number. In the latter part of the illness the former may fall below fifty per cent.

The Liver.

A prominent effect of the presence of typhoid bacilli in the body is the presence of minute spots of necrosis and inflammation in the liver. These spots were at first spoken of as lymphoid nodules and compared to the lymphoid hyperplasia in the intestines, mesenteric glands, and spleen. Attention was called to these minute nodules by Friedrich in 1859, and they were more fully described by Wagner in 1860. Hoffmann found them in thirty-eight out of two hundred and fifty cases, but they are probably more frequent. Some of these spots lie between the lobules, and consist of an increase of lymphoid and plasma cells with a proliferation of endothelium cells forming large phagocytic cells. Others lie within the lobules and show similar cells and, in addition, necrosis of these and of the liver cells. These changes have also been found in other infectious diseases. The nodules are so small that few of them can be distinguished by the naked eye. There is also considerable parenchymatous degeneration of the liver cells, varying in degree with the stage and severity of the attack. The cells are at first filled with albuminous granules, later with fatty granules and coarse fat drops, and they may ultimately break down. The periphery of the lobule is usually more affected by

these degenerative changes than the centre. In its gross appearance the organ is often reported intact, often as slightly changed, and often as showing distinct lesions. At first it is apt to be hyperæmic and slightly enlarged; later it becomes somewhat flabby and pale; as the result of the parenchymatous degeneration the lobular markings become less distinct. In severe and protracted cases the degeneration may reach so high a degree that the organ becomes small, flabby, of a grayish color, and suggesting somewhat the condition found in acute yellow atrophy.

Abscess of the liver is an occasional complication of typhoid fever; it may occur by direct extension of the ulceration of the larger bile ducts, as the result of septic thrombosis of the portal vein arising from ulcerative or suppurative intestinal or periintestinal inflammation, or as part of a general pyæmia.

Other Glands.

The *pancreas* may be a little enlarged with some apparent proliferation of the cells and some albuminous and fatty degeneration. The *salivary glands* are often swollen and show under the microscope some congestion and some cloudy swelling of the gland cells. Changes in the *thyroid* are rare. Curschmann found in 347 autopsies no case of inflammation of the thyroid, and in a large epidemic he found only 2 cases clinically. Griesinger found inflammation of the thyroid 4 times in 118 autopsies. Topfer found 3 abscesses in 927 autopsies. Liebermeister found inflammation 15 times in 700 patients; in 6 of these there were abscesses. Walther found that in 73 cases of acute thyroiditis 40 were to be referred to typhoid fever. The Eberth bacillus has been found a very few times in the inflamed gland. In several other cases the pyogenic streptococci and staphylococci have been demonstrated. Typhoid inflammation of the thyroid is more apt to occur at the beginning of convalescence or during the last week of fever. It is more apt to occur where there has already been a hyperplasia of the organ, and therefore especially in regions where goitre is endemic. Usually only a small part or a half of the organ is affected. The condition as a rule goes on to satisfactory healing. It may cause compression or displacement of the trachea or may perforate into it.

The Kidneys.

The quantity of urine is diminished during the fever and often much increased during convalescence. Urea and uric acid are increased; the chlorides during the febrile period are much diminished.

Albuminuria is said by some to be found in nearly every case, but most authorities report it as present in one-third to one-half of the cases. Hyaline casts are often found. The death rate is much greater in those cases which show albuminuria than in those which are free from it. It appears most commonly during the second or third week, rarely very late in the disease, but it may reappear or increase during relapses and exacerbations. The presence of albumin in rare cases lasts for a long time after the attack is over, and may continue for years without any other signs of nephritis except a few hyaline casts. In this respect it resembles some other acute infectious diseases. Very rarely hæmoglobinuria is seen at about the end of the second week. Klemperer has reported a case in which it occurred after recovery. The chemical change in the urine must also be noted, upon which depends the Ehrlich diazo reaction. There is commonly a greater or less amount of parenchymatous degeneration of the kidney. This is seen microscopically in an albuminous or fatty clouding of the epithelium of the tubules; later, a coarse fatty degeneration and breaking down of the cells. On gross examination early in the fever the kidneys appear hyperæmic; as the disease advances the organ commonly becomes enlarged, the cortex thickened, of a grayish-red or yellowish color. After a long, severe run of fever the kidney, like the liver, becomes smaller, more flabby, and of a lighter color. A well-marked nephritis is not common, occurring, according to Curschmann, in hardly one per cent. of the cases. A moderate degree of nephritis, not easily distinguished from a simple albuminuria, occasionally occurs at the height of the disease before the end of the third week, later it is much more rare. A few cases have been reported as appearing during the first week. It is less common in children than in adults, and less common in women than in men. In 25 cases nephritis occurred in patients under 15 years of age, 3 times; 16 to 25 years, 11 times; 26 to 35 years, 8 times; 36 to 45 years, once; 46 to 55 years, once; over 55 years, once.

Nephritis occasionally is quite severe and presents marked clinical symptoms; it may occur early in the second week or even at the end of the first week, and occasionally the trouble so dominates the clinical picture that the name of "nephrotyphus" has been given to a few cases. Death may occur from uræmia. In typhoid nephritis the interstitial tissue is usually but slightly involved. Small gray nodules similar to the "lymphoid nodules" or areas of focal necrosis seen in the liver have also been observed in the kidney. Cases have also been reported in which there were numerous miliary purulent foci, sometimes uniting to form abscesses of considerable size. Changes in the rest of the urinary tract are less common,

though pyelitis and cystitis occasionally occur. In some of these cases typhoid bacilli have been found in the urine. Inflammations of these tracts may be suppurative or diphtheritic, and the bladder also has been known under these circumstances to undergo suppuration and perforation.

The Lungs.

The marked tendency of the larynx to undergo destructive inflammation in typhoid has been spoken of above (p. 594). The trachea and the larger bronchi are rarely the seat of serious changes. There may be some congestion and catarrhal trouble and even a little erosion; there are not often real ulcers, and very rarely do these result in perichondritis, necrosis of the cartilage, or peribronchial suppuration. Some have reported the finding of diphtheritic membranes in the bronchi, and others extensive fibrinous tracheobronchitis. The smallest bronchi show during the entire febrile period a catarrhal condition which may result in atelectasis and lobular pneumonia. After a severe and protracted case of typhoid, and sometimes at the height of the fever, the posterior parts of the lungs show hypostatic consolidation. The swelling of the mucous membrane of the bronchi and the resulting atelectasis together with the weakness of the circulation and the influence of position are important factors in determining this condition. Out of 1,830 cases, in 121 there were signs of splenization or inflammatory thickening of the lower lobes. It is much less frequent in children than in adults, probably because the attacks are less severe in them. Inflammations of the lobar type are not infrequently observed.

As regards the bacterial agents which are active in producing these forms of pneumonia, in a considerable number of the cases of atelectasis and lobular pneumonia following bronchitis pyogenic streptococci and staphylococci have been found, but in a few cases typhoid bacilli. In the true lobar inflammations the Fraenkel pneumococcus is almost always found to be the cause, occasionally the Friedländer bacillus. There occur also mixed infections, as by the pneumococcus combined with a streptococcus. A less frequent simple infection in the pneumonia of typhoid is that by staphylococci. Chantemesse and Bruno and a few others have obtained pure cultures of the Eberth bacillus in lobar pneumonia, and cases of mixed infection have been described in which the Eberth bacillus was associated with streptococci and staphylococci. As independent or prominent exciters of pneumonia the streptococci seem to be more frequent than the staphylococci, producing lobular as well as lobar forms, and they are also found in

simple hypostatic splenization and in the aspiration pneumonias. The streptococci aspirated from the typhoid ulcerations of the larynx and laryngeal perichondritis may produce severe pneumonias, but the streptococcus pneumonia of typhoid is probably in most cases part of a general secondary septic infection. Pneumonias produced by streptococci and other pyogenic germs, being secondary infections, appear, as we would expect, almost exclusively in the latter part of the fever or in the period of convalescence. All of these forms of pneumonia may cause the development of an abscess, though this fortunately occurs but rarely. Abscesses may, however, arise in a purely metastatic way as the result of complicating pyæmia. It is probable that even the pneumonias due solely to the typhoid bacilli may go on to suppuration without the help of other germs.

More frequent than abscess is grangrene of the lung. This may be a secondary result of a lobar pneumonia, of a pyæmic, or of an aspiration pneumonia. It may also result from an arterial thrombosis as in other parts of the body. Particles of food may be drawn into the lungs in cases not well cared for, or particles from infectious, ulcerative, or suppurative affections of the mouth, pharynx, or larynx, and may give rise to this condition. Liebermeister found gangrene in fourteen out of twenty-three cases; Griesinger, seventeen times out of one hundred and eighteen; Curschmann, ten times out of two hundred and twenty-eight. Hemorrhagic infarction of the lung is not uncommon, as we might expect from the prevalence of changes in the blood-vessels, which we shall see later to be a prominent feature of typhoid disease. Such an infarction may result in resorption, cicatrization, or suppuration. Rarely it may be so extensive as to cause sudden death. Suppuration of the infarction may spread to the pleura and cause empyema.

Any considerable pleurisy or a pleurisy independent of pneumonia is rare. When it does occur, it is apt to be in the latter part of the fever or during convalescence, though it has been seen during the first week. The bacillus of Eberth has been found in pleuritic exudations, both serous and suppurative, but not in many cases. Westcott collected nine cases, in five of which the Eberth bacillus was demonstrated. A fibrinous pleurisy accompanying the different forms of pneumonia is not uncommon, and is supposed to be due to the same microorganisms. Pneumothorax is extremely rare and generally depends upon abscess or gangrene.

An important pulmonary complication of typhoid fever is tuberculosis, which may occur as part of a general miliary tuberculosis or as a local condition; occasionally an old apical tuberculosis which has been running a slow course flares up and extends during an attack of

typhoid. In typhoid pneumonia the tubercle bacillus has frequently been found with the Fraenkel pneumococcus with corresponding mixed histological conditions.

THE NERVOUS SYSTEM.

Lesions of the nervous system visible to the naked eye or even to be detected by the microscope are by no means prominent in typhoid fever. Meningitis occasionally occurs. In some cases with marked cerebral symptoms, an inflammation has been found microscopically which could not be seen with the naked eye, and consisted of a small-cell infiltration of the meninges with an extension of the process along the vessels into the brain substance. There may be various degrees of inflammatory change from this up to marked suppuration. But there is no doubt that in many cases in which the cerebral symptoms are severe and properly arouse the suspicion of inflammation of the membranes there is simply a toxic condition due to the poisonous products of the invading bacteria. Various microorganisms have been found in the different cases of meningitis. The bacillus of Eberth has been obtained in some cases. Keen has collected 15 cases in which the bacillus of Eberth was reported to have been found; in 12 it was expressly stated that the bacillus was found in pure culture. Wolf found in 174 cases of meningitis examined bacteriologically 2.87 per cent. containing typhoid bacilli. Sometimes, especially when associated with fibrinous pneumonia, it is probably due to the pneumococcus of Fraenkel. At other times the germ of genuine epidemic cerebrospinal meningitis, the micrococcus meningitidis intracellularis, has been obtained, and the causal connection between this germ and some cases of meningitis complicating typhoid fever is further supported by the frequency with which the two diseases occur in the same patient in localities where cerebrospinal meningitis and typhoid fever prevail. The pyogenic streptococci or staphylococci, either alone or as a mixed infection with other germs, may cause a suppurative meningitis. Tuberculous meningitis has been seen in a very few cases following typhoid. Inflammation may spread to the membranes from an otitis media by way of thrombosis and caries of the petrous bone, inflammation of the sinuses and a meningophlebitis. These meningeal complications may begin early in the attack, but more frequently begin in the latter part of the febrile stage or the first part of convalescence. The cases which are due to a simple infection with the typhoid bacillus are more apt to occur early in the fever. Those due to a secondary infection with pyogenic germs are naturally more apt to occur late. A tuber-

culous meningitis, when it occurs, appears usually, if not always, during convalescence. Those which occur early are rarely fatal, probably because they are more frequently due to the Eberth bacilli; those which occur as later complications are apt to be more severe and are very likely to come to autopsy. Hemorrhages in the membranes or in the brain substance are very rare. Phlebitis of the sinuses, the intracranial veins, and the cerebral arteries has been occasionally observed.

Hawkins has collected seventeen cases of hemiplegia complicating typhoid fever in children; of these, two were fatal, and in each there was a thrombus in the middle cerebral artery. On the other hand, in one hundred and twenty cases of cerebral palsy in children, collected by Osler, not one was a complication of typhoid fever, and of one hundred and sixty cases collected by Wallenberg, only four were typhoid cases.

Cerebral abscesses occasionally occur. They may result by extension from an otitis media or metastatically from abscesses in other parts of the body or from bedsores.

Lesions of the medulla oblongata or spinal cord are almost unknown. A few cases of bulbar hemorrhage and softening have been recorded. Several cases of multiple sclerosis of the cord have been observed both clinically and anatomically. A few cases of spinal paralysis in children have been seen during typhoid. There are two instances on record of autopsy in cases in which during typhoid fever or convalescence from it the clinical picture of Landry's acute ascending paralysis was present. In the cord of one case typhoid bacilli were found abundantly by the microscope and obtained by cultures; in the other no significant changes could be found.

Neuritis may occur and may be extensive.

The Circulatory System.

Typhoid infection attacks with especial virulence certain portions of the circulatory system, and there is no part that may not be seriously affected. It is especially the minute lymph channels that are attacked. The changes in these places have already been noted (p. 785). The changes which we frequently find in the large vessels, especially the veins, are probably due in large part to similar processes. The proliferation of cells in and beneath the endothelium, which has been so thoroughly studied by Mallory, and their subsequent degeneration with the consequent formation of fibrinous thrombi offer a very reasonable explanation of the thromboses which occur so frequently in the veins of typhoid patients and often in the arteries. We have in addition the feebleness of the circulation due to the general prostra-

tion and degenerative changes in the heart, and we may have additional and deleterious agents working in the same direction where, as so frequently occurs late in typhoid fever, there is a secondary infection with pyogenic and perhaps other bacteria. Thrombosis of the large veins of the leg with the well-known symptoms of phlegmasia alba dolens is a common occurrence during the later stages of typhoid fever, and especially during convalescence. It sometimes comes on with an exacerbation of fever, with considerable pain in the region of the crural and iliac veins, and with redness and tenderness along these veins, from which we must conclude that it is not always a simple thrombosis, but depends upon, or at least is associated with, an inflammatory condition of the venous wall. The presence of the Eberth bacillus in typhoid phlebitis has not been satisfactorily established as a regular occurrence. Pyogenic cocci have been observed. This accident occurs commonly during convalescence. As is the case in other infectious diseases, such as puerperal fever, pneumonia, septicæmia, pyæmia, tuberculosis, and malarial fever, venous thrombosis occurs most frequently in the lower extremities, and more frequently in the left leg than in the right. Keen's figures for venous thrombosis of the legs and thighs are: Left side, sixty-nine cases; right side, twenty-three cases; both sides, seven cases. Next to the pulmonary and saphenous veins, the popliteal and tibial veins follow in frequency. Phlebitis and periphlebitis have been seen in typhoid cases in old varicose dilatations of the veins of the leg. It is occasionally seen also in other parts of the body, as in the subclavian and the axillary. The thrombosis may extend from the pulmonary vein into the iliac and the vena cava, and even into the right artery. Death follows in the latter case, and may be caused by embolism of one of the main pulmonary arteries or one of the cerebral arteries. Venous thrombosis may also have some influence in producing gangrene of various superficial parts, but it is much more commonly produced by arterial changes. This venous complication is often distressing to the patient, and usually greatly prolongs convalescence and may impair the usefulness of the limbs for a long time, but it usually ends in recovery without serious consequences.

The arteries are much less frequently affected than the veins, but their affection is more apt to lead to serious consequences, especially gangrene. Typhoid gangrene is most frequently seen in the lower extremities, and usually on one side only. It may be confined to the toes or may involve large parts of the limb. In the upper extremities the lesion is extremely rare, though it is sometimes seen there, and may involve other superficial parts, as about the neck or the mouth or the genitals. The female genitals are more apt to suffer than the

male and there may be extensive destruction of tissue, opening the urethra, the bladder, or the rectum, or lighting up a peritonitis. The rarity of typhoid gangrene may be seen in the following figures: Hoelscher, in 2,000 cases, found none recorded; Boettke, in 1,420 cases, found 4 recorded, limited to the toes; Keen and Westcott have collected 133 cases. It usually occurs late in the febrile period or as an early sequel during convalescence. The ages at which gangrene occurs appear from the following figures given by Keen: Under 15 years, 26; from 15 years to 25 years, 64; after 25 years, 50. Its distribution appears in these figures: Legs, 126; face, neck, trunk, 47; genitals, 20; anus, 5; nose, 10; ears, 6. Rarely it is symmetrical, reminding one of Raynaud's disease. A peculiar arthritis seems to cause in rare cases a superficial inflammation about the joints.

The minute spots of necrosis, produced particularly in the liver, but also in the kidney and other organs through obstruction of the circulation by large proliferated endothelial cells, have already been described.

The Heart.

Degenerative changes in the heart muscle have been frequently observed. The degeneration may be an albuminous, a granular, less commonly a fatty, occasionally a hyaline or waxy degeneration, but even in some cases in which death has occurred after a severe course of high fever the muscle fibres may show little or no change. Endocarditis and pericarditis are infrequent. The typhoid bacilli have been found in endocardial vegetations. Pericarditis may result as an extension from a neighboring pneumonia or as a part of the secondary pyogenic infection. An interstitial myocarditis also occurs, with round-cell infiltration running along the vessels between the muscle bundles. Abscess in the heart wall has been reported. Changes in the coronary arteries such as to produce anginal attacks or to be recognized by the naked eye at autopsies are very rare. Inflammation of the lining of the small vessels has been observed, and thrombi sometimes form in the cavities of the heart. Portions of the latter may be washed away producing infarctions, most commonly in the kidney or spleen, and, as is the case with fragments of venous thrombi, may in rare cases produce serious embolism of pulmonary or cerebral vessels.

The Osseous System.

The bones are peculiarly liable to suffer from the action of the typhoid bacilli. The latter have been found in abundance by many observers in the medullary tissues of the bones and in the inflammatory

products of their lesions. They have been found lurking here for many years after the attack of fever, associated with more or less interrupted symptoms of trouble in and about the bones. Moreover, Ponfick and Mallory find changes in the medulla which closely resemble the characteristic typhoid changes in the structure of the lymphoid tissues of the intestines, mesenteric nodes, and spleen. The lesions are most commonly periostitis with resulting necrosis or abscess; they have been classified by Keen as follows: necrosis in 85 cases, caries in 13, periostitis in 110, ostitis in 12, osteomyelitis in 10, exostosis in 1, granuloma in 2, uncertain in 4. In some cases the trouble is not extensive and subsides without any permanent injury. Besides abscesses and necroses of the bones perforation into a joint may occur. The bone complications appear commonly late in the disease and often have appeared long after convalescence had been apparently established. They are said to have occurred, in 186 cases, in the first two weeks, 16 times; from the third to the sixth week, 66 times; months or years after the fever, 104 times.

The long bones, especially the femur and the tibia, are most frequently attacked, occasionally the ribs and sternum. In 215 cases the affection occurred in the lower extremities (especially the femur and tibia), 112 times; in the trunk (especially the ribs), 48 times; in the upper extremities (especially the humerus and ulna), 41 times. In 166 cases it occurred 127 times at thirty years or under, and 39 times over thirty years. It is especially apt to attack young people near the time of puberty. In 186 cases it occurred 123 times in males and 63 times in females. There may be only one spot of such trouble, or it may be scattered in various parts of the body. In young children it more often begins in the region of the epiphysis. The evidence so far collected points strongly to the view that suppuration in the bone is usually due to the typhoid bacillus, but there are cases of mixed infection. These inflammations occasionally occur at the site of old lesions, and cases have been observed in which long after the attack of fever a periosteal inflammation was set up as an immediate result of injury. In some such cases the typhoid bacilli have been cultivated, and it seems probable that the bodies of those convalescent from typhoid fever may for a considerable time contain foci of the bacilli which may never produce further trouble or after some injury may start up an inflammation. Colzi found by experiment that an injection of a pure culture of typhoid bacilli in a rabbit's ear gave negative results, but the same injection preceded by subcutaneous fracture of the bone resulted in an abscess in eleven out of fourteen cases.

Typhoid affections of the *joints* may be of three kinds: proper

typhoid, rheumatic, and septic. Typhoid arthritis proper may be limited to one joint or may affect several. The lower extremities are more frequently involved than the upper, and especially the hip-joint. Suppuration rarely follows. Keen has collected eighty-four cases; in forty-three of these spontaneous dislocation occurred, forty times in the hip.

The Skin.

The skin shows characteristic lesions, especially in the form of the rose-spots which will be discussed in the article on the symptomatology. Neuhaus and Reutmeyer report the finding of typhoid bacilli in the blood taken from these spots. Of secondary importance are the "taches bleuâtres," urticaria, erythematous, papular, and miliary eruptions. Herpes is much less common than in certain other infectious diseases. Erysipelas is very uncommon, but furuncles and small abscesses in the skin are quite frequent. These latter occur especially as the fever is falling and during convalescence. They are sometimes sufficiently extensive to retard convalescence and even dangerously to weaken the patient. As many as sixty to eighty small superficial abscesses have appeared in a single patient; they are seen most commonly on the back of the trunk and after that on other parts of the trunk, on the thigh, and on the upper arm. This complication is thought by Curschmann to be more frequent when frequent cold baths are used.

One of the most unfortunate sequelæ of typhoid appearing at the surface of the body is the occurrence of bedsores. This has fortunately become much less frequent as our methods of treatment, especially of nursing, have improved, and when it does occur is generally a reflection upon the physician or the nurse. In some collected groups of cases it occurs in one to two per cent. of the patients. Its favorite site is in the sacral and gluteal regions; less commonly on other projections of the body upon which the weight of the patient falls, as the heels, shoulder blades, spinous processes, and the back of the head. It appears late in the attack and may extend into convalescence. It most commonly results from pressure and a lack of cleanliness, but it may follow eruptive lesions of the skin, which in turn may be due to a lack of cleanliness. It is sometimes observed as a result of the profound general disturbance of nutrition, and not necessarily in the places of most severe pressure, and sometimes it is more intense beneath the skin than in the skin itself. This form is perhaps most frequently seen in the neighborhood of the coccyx and the anus. The occurrence of gangrene as the result of changes in the blood-vessels has been mentioned already. It sometimes occurs also

as the result of trauma, either accidental or therapeutic, as when counter-irritation—heat, or cold—has been applied. The occurrence of bedsores and gangrene is of extreme importance because they may furnish pyogenic and other bacteria the means of entrance into the body, producing mixed infections, pyæmia, etc.

The *hair* as a rule, the *nails* occasionally, may be affected in typhoid fever. The loss of hair to a greater or less extent occurs in most of the cases. It is usually the hair of the head that is lost, rarely that of the beard, almost never that of other parts of the body. There have been cases reported in which the entire hair of the whole body has been lost. It usually occurs late in the disease or during convalescence, sometimes even after the patients have resumed their ordinary pursuits. The hair is almost invariably recovered. The new hairs are usually thicker, firmer, and without lustre; they are often elliptical on cross section, which may be the cause of curling. The nails after a severe attack are sometimes found to be thin and friable, occasionally they are lost, and sometimes transverse ridges are formed during the attack.

The Muscles.

The muscles often show atrophy or degeneration. The latter may be granular, albuminous, fatty, or waxy. This waxy degeneration from the second to the fourth week often produces a somewhat firm consistence of the muscles and a spotted or streaked grayish-red or waxy-gray appearance on section. The tissue often becomes unusually friable, more commonly so than in any other infectious disease. The tongue, according to Hoffmann, not infrequently shows a waxy degeneration.

Abscesses have been frequently found in and about the muscles. In many cases pure cultures of the Eberth bacilli have been obtained from such abscesses. Hemorrhages may also occur in and about the muscles.

TYPHOID FEVER.

(SYMPTOMATOLOGY AND TREATMENT.)

BY

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NEW YORK.

TYPHOID FEVER.

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SYMPTOMATOLOGY.

General Clinical Course.

THE *period of incubation* of typhoid fever appears to vary within rather wide limits. The usual interval between exposure to the infection and the onset of the disease is from eight to fourteen days. Its duration is probably largely dependent upon the susceptibility of the patient and the intensity and quantity of the poison ingested. Sometimes the period of incubation appears to be extremely short, as in three cases reported by Griesinger in which the attack commenced on the day following exposure. Some writers are inclined to doubt the value of these observations, as, in their opinion, the diagnosis was uncertain. It is true that few details of the cases are given, but Griesinger apparently had no doubt of the nature of the disease. He himself was one of the three individuals affected, and there seems to be no good ground for disputing the correctness of his diagnosis. In another instance, related by Murchison, twenty out of twenty-two schoolboys developed the disease within four days of exposure. On the other hand, authentic cases are reported in which the symptoms did not appear until three or four weeks had elasped after a definite single exposure to the exciting cause. Perhaps the manner in which the contagion is taken into the body is a factor in the rapidity with which it affects the system. Some observers believe that the germs produce their effects more quickly when they are inhaled than when they are introduced into the alimentary canal with the food or drink. It is possible, also, that the germs may lie latent at some point in the body for a greater or less length of time and then suddenly display their pathogenic properties. Kolisko has shown conclusively that this is sometimes the case in diphtheria. After a careful consideration of all the evidence we are justified, I think, in concluding that the usual period of incubation of typhoid fever is from eight to fourteen days. In rare instances the duration may not exceed one or

two days. Still more rarely the interval between exposure and the development of the disease may extend to three or even four weeks.

Typhoid fever is generally a disease of slow development. The onset is often so gradual that it is difficult to determine the day upon which the illness began. The patient feels languid and disinclined to mental exertion. He has headache and pains in the back and legs and a general sense of weariness. His appetite is impaired and his sleep restless or disturbed by dreams. There may be nausea or even vomiting, and either diarrhœa or constipation may be present. There is seldom a decided chill, but the patient may complain of sensations of chilliness or slight feverishness. These slight symptoms are usually classed as prodromes and assigned to the stage of incubation. The patient, as a rule, does not feel obliged to go to bed, and keeps at work in spite of his indisposition to exertion. As his malaise increases, however, he seeks medical aid, and the thermometer then usually shows a degree or more of fever and the illness may be said to have begun.

The duration of uncomplicated typhoid fever is from three to four weeks. The disease may be divided into three stages: the stage of invasion, the stage of continued fever or the fastigium, and the stage of decline. The stage of invasion lasts from five days to one week, the stage of continued fever one to two weeks, according to the severity of the case, and the stage of decline one to two weeks. Some observers date the beginning of the disease from the day the patient takes to his bed, though they admit with Flint that the illness must often have progressed to the third or fourth day before the confinement to bed begins. It seems more rational to date the onset from the day when a decided elevation of the temperature, with its accompanying symptoms, is first noted by either patient or physician.

First Week.—With the advent of fever the patient begins to feel really ill. His weakness increases from day to day, his appetite is lost, and he complains of constant thirst and severe headache. The tongue is covered with a white coat, except the edges and tip, which are red, and there may be slight epistaxis. There is often diarrhœa, especially if a cathartic has been given at the beginning of the illness. Some patients suffer from deafness and ringing in the ears. In many cases the disease begins with a cough and signs of bronchitis. The spleen is usually enlarged and can often be detected by palpation. The temperature continues to rise steadily, being a degree or more higher each evening than on the evening before, until towards the end of a week from the day of onset it reaches 103° or 104° or even 105°. The pulse rate is quickened, but not always in proportion to the fever. It ranges from 90 to 110, and is soft and sometimes dicro-

tic even at this early period. As a rule the patient is forced by his increasing weakness to take to his bed some time during this week.

Second Week.—The second week is marked by a persistence or an increase of all the symptoms of the first week, as well as by the addition of certain new features. The temperature each evening maintains with slight variations the maximum height reached at the end of the first week, remitting in the morning a degree to a degree and one-half, the remissions being less marked in severe cases. There is less complaint of headache, the patients becoming apathetic and somnolent, and more or less delirious, particularly at night. The face looks dull, the tongue is tremulous, and the prostration of the patient is marked. Bronchitis is usually present and the cough may be very distressing. There is more or less tympanitic distention of the abdomen, with tenderness on pressure in the region of the cæcum. There is usually diarrhœa, the patient having from two to six loose, yellow stools in the twenty-four hours. In some cases, however, there is constipation from the beginning to the end of the disease. Between the seventh and twelfth days the characteristic eruption appears. This consists of small, circular, slightly elevated, rose-red spots, disappearing on pressure. The spots are few in number as a rule and are found on the abdomen, chest, and back. They are usually developed in successive crops. The skin is generally dry, but there may be profuse perspiration, especially at night, accompanied by sudamina, followed in time by desquamation.

Third and Fourth Weeks.—From the fourteenth to the sixteenth day in cases of moderate severity the symptoms begin to improve. The first sign of improvement is usually furnished by the temperature. The morning remissions become more and more decided, though the evening rise remains the same for several days. Soon, however, the fever declines in the evening also, and towards the middle or end of the fourth week the temperature is normal both morning and evening. With the decline of the temperature the general symptoms improve as a rule. The tongue grows moist and tends to become clean, the diarrhœa ceases and the appetite returns. The patient sleeps soundly and awakes with clear mind. His strength also returns gradually, though convalescence is slow even in mild cases and may be interrupted by complications. Occasionally, also, after perhaps a week or more of normal temperature, the fever may return and the patient has a relapse attended with all or most of the symptoms of the original attack, though usually in a milder form.

In severe cases the fever fails to decline during the third week. In fact the usual morning remissions may be less marked and the patient soon shows the effect of the continued high temperature and

the prolonged toxæmia. The apathy and somnolence increase during the day and the delirium at night becomes more severe and more active. In some patients delirium predominates by day as well as at night, and they may require constant watching and restraint. In the intervals of active delirium the patient lies motionless in bed, sometimes muttering to himself, oblivious to his surroundings. He asks for nothing, but will drink if milk or water is put to his lips. The tongue becomes dry and brown and covered with sordes, or red and glazed in appearance. The lips are dry and cracked, and the teeth also collect sordes unless carefully looked after. The face is dull and dejected. The urine and fæces may be passed involuntarily. The abdominal symptoms also become more marked. The tympanitic distention increases and the diarrhœa is usually profuse. The pulse is rapid and weak. The first sound of the heart grows feeble. The bronchitic signs increase and the catarrh may extend to the smaller tubes. All these symptoms may continue into the fourth week and then diminish and the patient slowly recover. Or various complications, to be described later, may arise and prolong the disease or cause the death of the patient. In some cases death results from simple exhaustion or cardiac failure. There may also be intestinal hemorrhage, or perforation of the bowel with resulting peritonitis and collapse. In cases which are severe from the outset, all the above clinical phenomena may be observed as early as the second week of the illness. Typhoid fever appears under so many forms that it is scarcely possible to describe and group together all its various manifestations in an article of reasonable length. I shall, therefore, pass on to a consideration of its chief features and symptoms

Analysis of Special Symptoms.

The Face.

The physiognomy in typhoid fever presents as a rule nothing characteristic in the early stages. The cheeks may be flushed, particularly at the time of the afternoon rise of temperature. As the disease progresses, however, in cases of any severity the expression of the face becomes dull, the skin pale, and the eyes become heavy. There is often a circumscribed pink flush on one or both cheeks. The pupils are generally dilated throughout the illness, but according to Murchison they may be narrowly contracted when there is complete unconsciousness. There is never the dusky face with injected eyes as in typhus fever. In severe cases attended with delirium the patients often have an anxious look during their semi-lucid intervals. When

there is great prostration, and the patient falls into the so-called typhoid state, his appearance is very characteristic. The facial muscles share in the weakness of the general muscular system of the body and give a peculiar relaxed, dejected expression to the face—the typhoid facies. At the same time there is often tremor of the muscles of the cheeks and lips.

Temperature.

The range of the temperature in typhoid fever is one of the most characteristic features of the disease. It often enables us to make a diagnosis when the other symptoms are absent. It is also of great importance in prognosis and furnishes valuable indications for treatment. The duration of the fever varies greatly in different cases, but as a rule it lasts for at least three weeks. The course of the fever falls naturally into three periods, corresponding to the different stages of the disease. During the stage of invasion there is a gradual ascent, the curve rising steadily in a step-like fashion, as shown graphically in Chart No. 1. From morning to evening the temperature rises about one and one-half to two degrees, and from evening to morning falls again about one-half to one degree. Thus the temperature each morning and each evening is about one degree higher than at the corresponding hours on the previous day.

If observations are taken at frequent intervals throughout the twenty-four hours it will be found that the temperature begins to rise about noon, and attains its maximum between 5 and 11 P.M. About midnight it begins to fall and reaches its lowest point between 6 and 8 A.M. It is important in typhoid fever to take the temperature at least as often as once in three hours if we wish to know the extreme variations during the twenty-four-hour period. In some cases, for example, the maximum is regularly attained at nine o'clock in the evening and the minimum at the corresponding hour in the morning. In other cases the extremes will be found an hour or two earlier. Again, the maximum and minimum will be observed at different hours on different days in the same case (see Chart No. 2). Occasionally, but very rarely, the highest temperature is reached in the morning and the lowest in the evening. It is the rule, however, in typhoid fever, as in other diseases, that the rise is in the evening and the fall in the morning. The steady ascent of the temperature continues from day to day, as above described, until at the end of a week or even a day or two earlier it reaches a maximum of 103° to 105° in the evening. This evening elevation is maintained with slight variations throughout the next

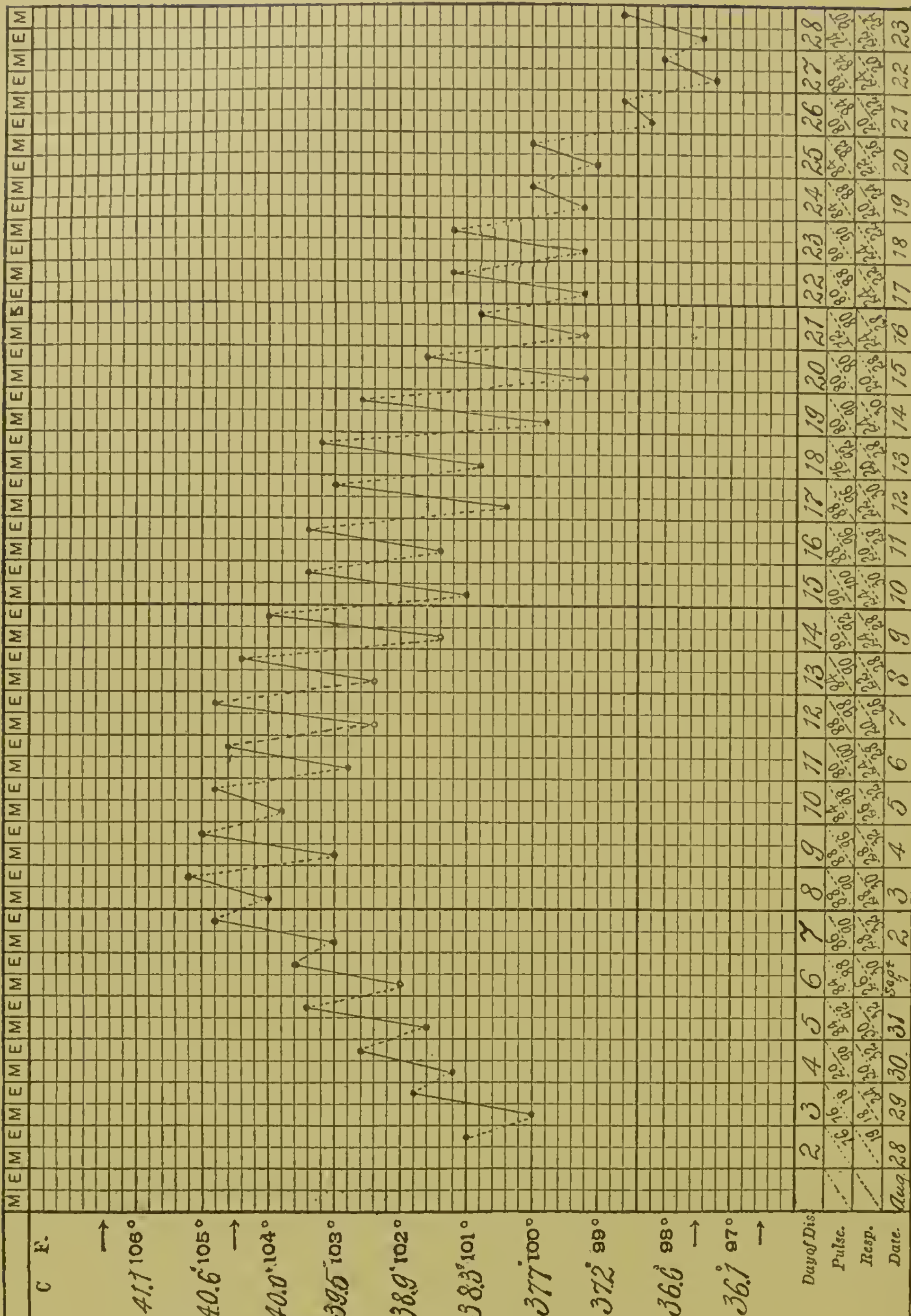

CHART No. 1.—Showing the Temperature Curve in a Typical Case of Typhoid Fever of Moderate Severity. The broken lines denote the night temperatures.

stage, the fastigium. The morning remissions, also, are less decided during the first part of this period, so that the fever is almost continuous. There may be less than one-half of a degree's difference between the morning and evening temperatures. During the latter half of the fastigium, in favorable cases, the morning temperature begins again to remit, the remissions becoming more and more marked.

The evening temperature remains at its previous level, so that the curve now assumes an intermittent form. The difference between the morning and evening temperatures at this period may be as much as four or five degrees. The duration of the fastigium varies from one to two weeks, according to the severity of the case. In very grave cases the duration may be much longer, even as long as four or

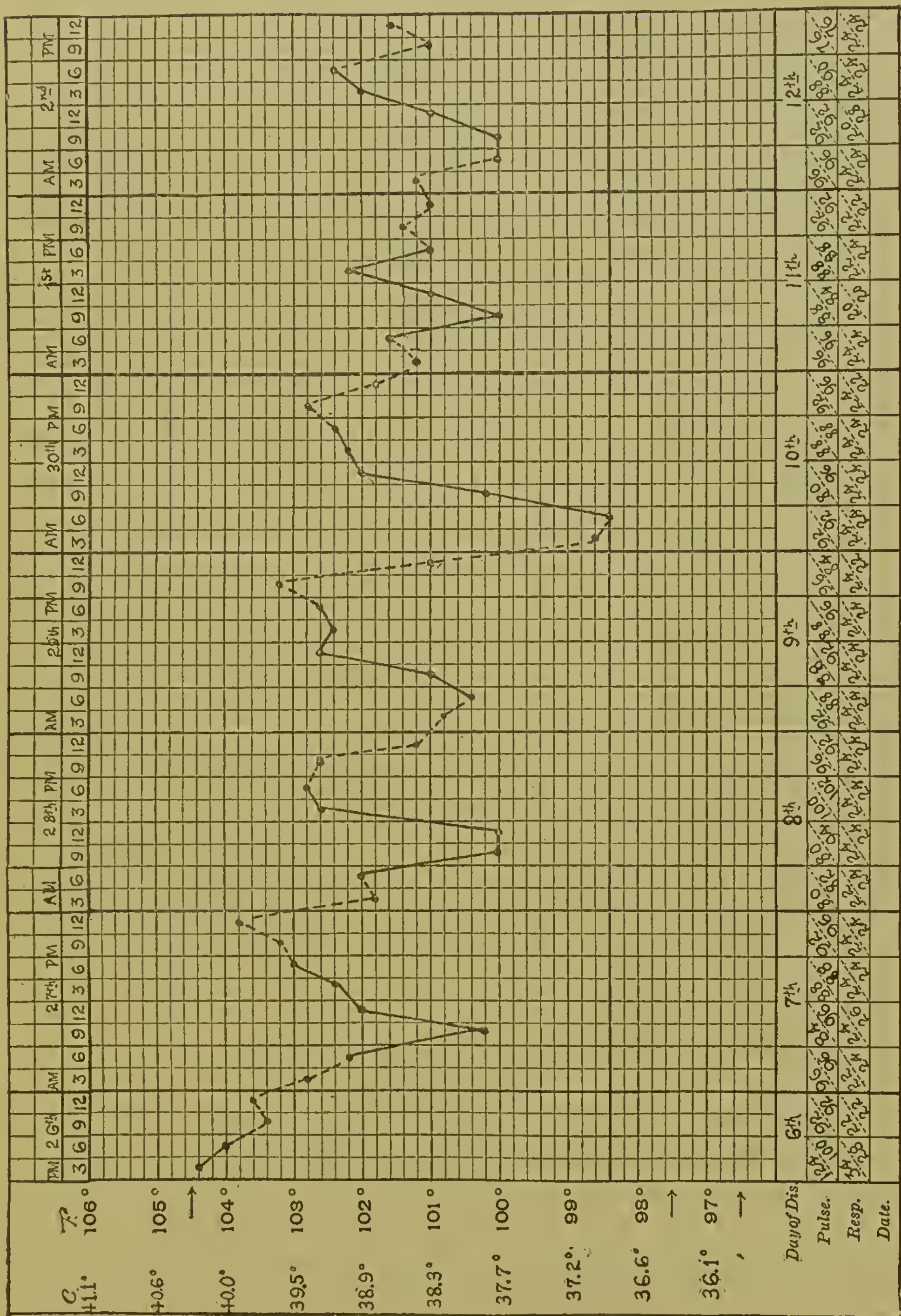

CHART No. 2.—Showing Extreme Variations of Temperature during the Twenty-four-Hour Periods. The broken lines denote the night temperatures.

five weeks. Its termination is indicated by a lessening of the fever in the evening; at the same time the morning remissions become more marked. The fever now declines in the step-like manner in which it rose, but usually more gradually. From evening to morning the temperature falls from two to three and one-half degrees, and from

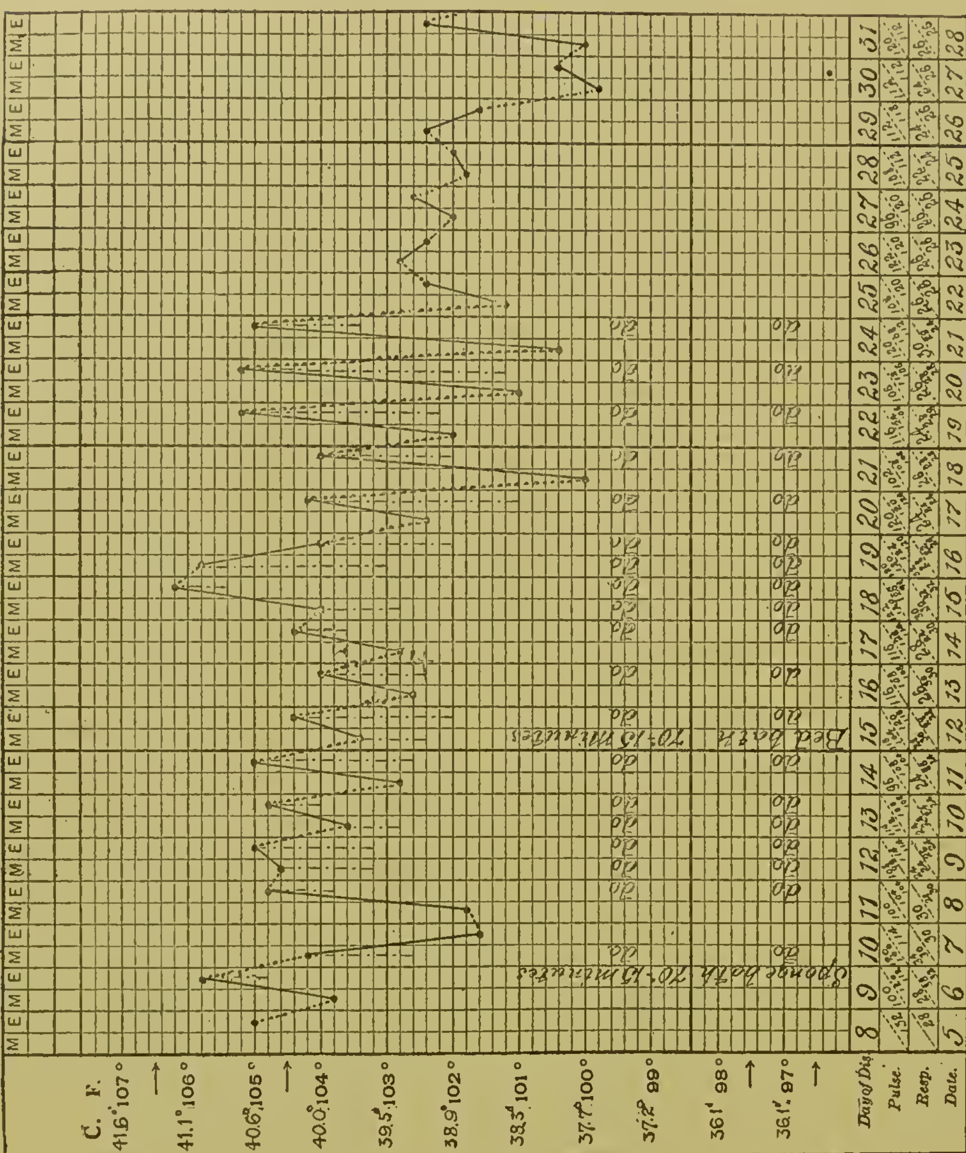

CHART No. 3.—Severe and Protracted Case of Typhoid Fever. Death occurred on the fifty-fifth day from exhaustion. The dotted lines indicate night temperatures.

morning to evening rises again from one and one-half to three degrees. Thus the evening exacerbation is each day from one-half a degree to one degree less than on the preceding evening. The stage of decline is, as a rule, much less regular than the stage of invasion and may last from ten days to two weeks, even in the absence of complications. The temperature is also very liable to rise suddenly from

very slight causes, such as emotional excitement or a slight indiscretion in diet. In such cases the rise is usually temporary and is termed a recrudescence and should not be confounded with the fever of relapse. At the end of this period the temperature is generally subnormal on one or two days. Convalescence cannot be considered as

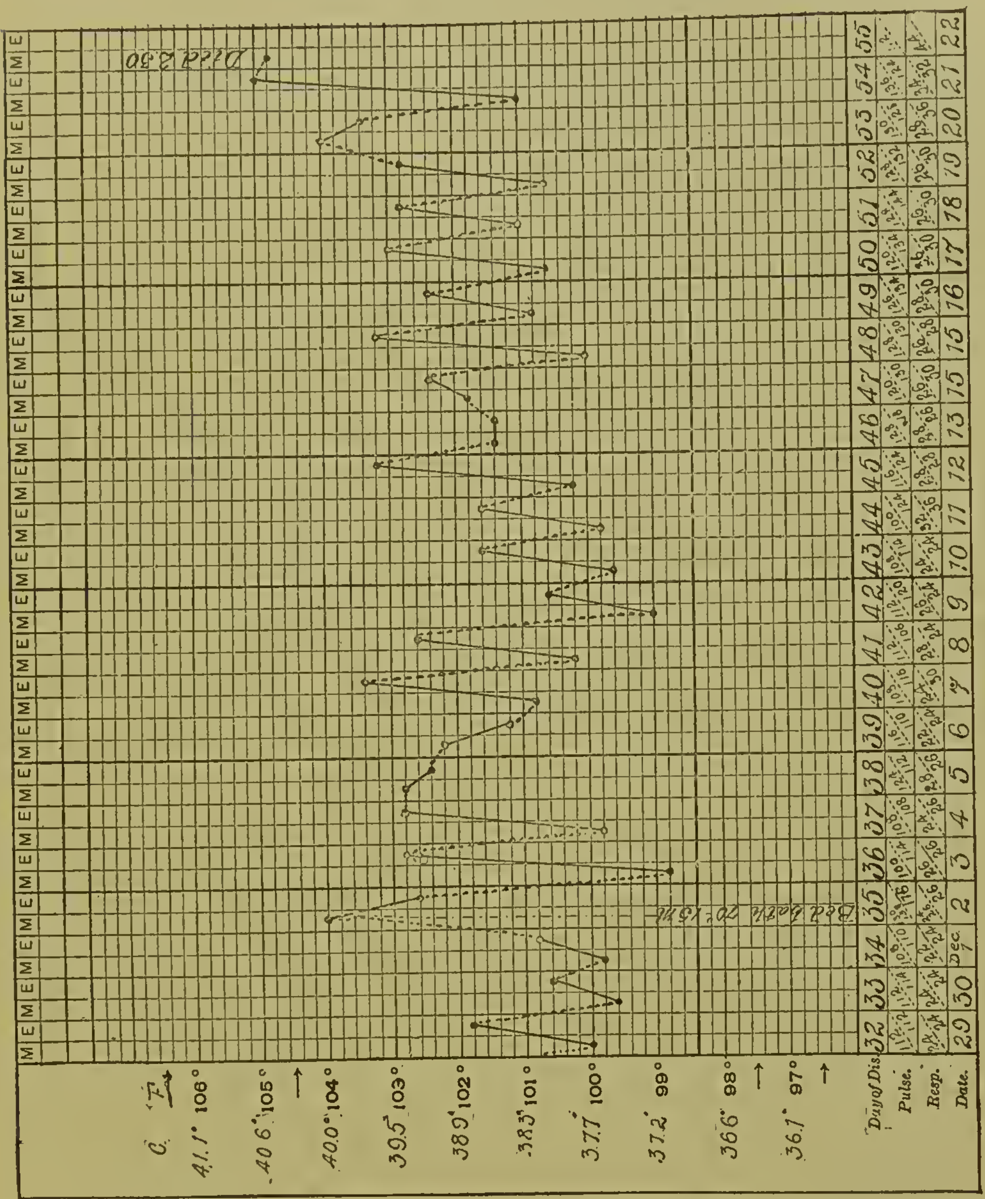

CHART No. 3.—Continued.

established until the temperature has been normal both morning and evening on several successive days.

The above description of the range of temperature in typhoid fever has been made sufficiently broad to include a considerable proportion of the cases ordinarily seen in practice. There are, however, many variations from this picture, some of which call for especial

mention. The stage of invasion is the most regular in its course. Unfortunately patients are seldom under observation during the whole of this period. This is especially true of hospital patients. Occasionally in private practice a case is met with at the beginning of this stage and the gradual ascent of the temperature may be observed (see Chart No. 1). In rare instances there is a sudden onset with chill and high fever, such as occurs in other acute infectious diseases. Sometimes this abrupt onset is more apparent than real, as in the two following interesting cases reported by Pepper:

A young girl of nineteen was taken suddenly ill in the night with vomiting, and the next morning had a temperature of 105°. On the following morning her brother, a boy of fifteen, was taken ill, and before night his temperature reached 104.6°. The girl, on subsequent inquiry, stated that she had not felt quite well for at least a week, but twenty-four hours before the onset she had been to a large dinner-party. The boy had continued to bathe in the ocean and to play tennis until the day preceding the attack. Pepper believes that had the temperature been taken regularly during the previous week, some ascending fever would have been found, since in both cases a profuse eruption appeared within thirty-six hours of the apparently abrupt onset, indicating that the seventh or eighth day of the disease had probably been reached. Yet for the purposes of early diagnosis the attacks seemed as sudden as though of acute gastritis. There are other rare variations from the usual initial period which will be referred to later in the description of the different forms of typhoid fever.

The fastigium presents the most frequent variations from the typical temperature curve. In very mild cases this period may be entirely wanting, the stage of invasion being immediately followed by a gradual defervescence. In other cases the temperature may be remittent or even intermittent throughout the whole of the fastigium. These atypical forms are sometimes found in groups, and under conditions excluding any possible malarial influence. Strümpell cites a number of cases observed by him during an epidemic in Leipsic, in which normal morning temperatures were followed by afternoon exacerbations reaching 104° or more. Sometimes at the end of the first week of the fastigium the temperature, instead of showing a tendency to remit, ascends to a higher level. This is always an indication of a grave degree of infection. An almost continuous high temperature is also of unfavorable import. High evening temperatures can be borne comparatively well provided the remissions in the morning are marked. Sudden temporary remissions or elevations of temperature are observed at some time during this period

in almost all cases of typhoid fever. A spontaneous remission without obvious cause is often noted from the seventh to the tenth day of the disease. A severe intestinal hemorrhage may be attended by a sudden and very marked fall of temperature (see Chart No. 4). Cases have been reported in which the temperature fell as much as nine or ten degrees. A fall of four or five degrees is not at all uncommon.

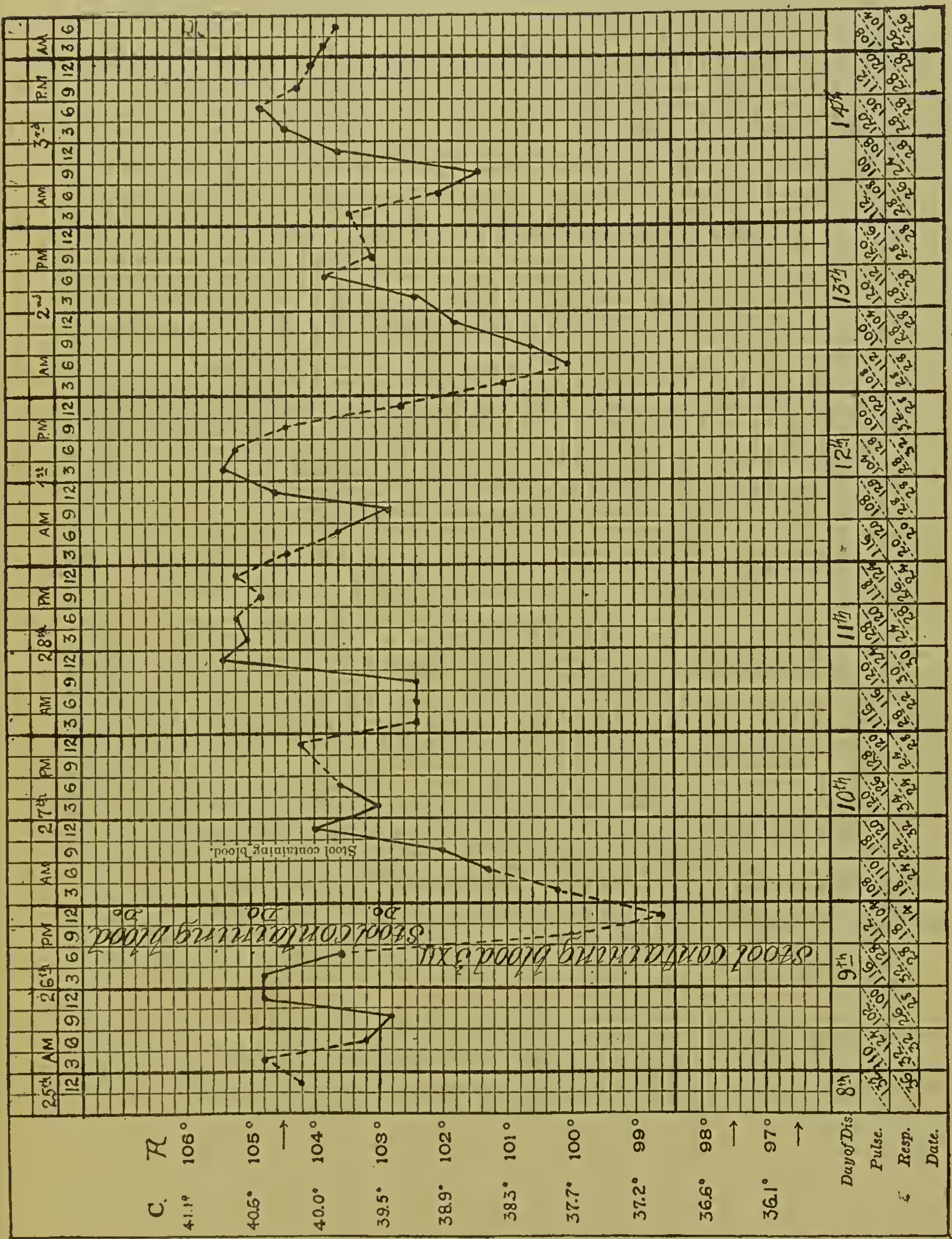

Chart No. 4.—Showing a Rapid Fall of Temperature following Intestinal Hemorrhage. The broken lines denote the night temperatures.

The temperature usually rises again and often to a point higher than its previous level. Perforation of the intestine is also sometimes accompanied with a sudden depression of the temperature. Occasionally the onset of a complication, such as lobar pneumonia, may be indicated by a chill and temporary fall of temperature. Usually, however, the occurrence of complications is signalized by a marked exacerbation of the temperature.

In cases of moderate severity the stage of decline follows the fastigium at once. In severe cases, on the other hand, the temperature pursues an irregular course for several days before definite defervescence sets in. This period has been called by Wunderlich the "ambiguous period" or the "period of changing fortunes." These cases usually run a protracted course and complications are liable to occur at any time. The defervescence of typhoid fever, as has been said, is usually gradual. Occasionally, however, but very rarely, the temperature falls by crisis. This period is especially liable to be interrupted by complications which may prolong it several weeks. Very slight causes may send the temperature up several degrees. Indiscretions in diet are the most common causes of these temporary recrudescences of fever. Even when convalescence has apparently been well established, the taking of the first solid food may be followed by a considerable rise of the temperature. The subject of relapses will be discussed later in a special section.

The Skin.

The skin is dry as well as warm in typhoid fever, the warmth varying with the elevation of the temperature of the patient. The dryness of the skin is not usually constant throughout the disease as there is sweating, more or less profuse, in most cases. The tendency to sweating becomes more decided as the disease progresses. The sweating generally occurs during the night or in the early morning with the remission of the fever. In cases marked by continuous high temperature sweating is rare. On the other hand, the sweating is not always accompanied with a fall of the temperature and sometimes occurs when the fever is highest.

The Eruption.

The eruption in typhoid fever is characteristic and its study is second only in importance to that of the temperature. The eruption consists of isolated lenticular rose-colored spots, slightly elevated above the surface of the skin. They are developed in suc-

cessive crops at intervals of three or four days. Each spot lasts from three to five days, gradually fading as fresh spots continue to appear. They vary in diameter from one to two lines, and have sharply defined borders. They are soft and disappear on pressure, returning promptly when the pressure is removed. In exceptional cases a minute vesicle may be seen at their apex. They are never indurated and are never converted into petechiæ, according to Murchison.

The number of spots is usually small, but varies greatly in different cases. Generally only a few are to be observed at one time, and sometimes only three or four spots are to be found throughout the whole course of the disease. Occasionally the eruption is very profuse and then the edges of two or three spots may touch each other. They never, however, become really confluent or merge into each other so as to form patches. Murchison has counted as many as one thousand spots in a single case at one time. The spots are said to be less numerous in children than in adults.

The spots are most commonly situated on the abdomen and lower part of the chest in front. They are also often found on the back and sometimes on the extremities. Occasionally the rash covers the entire body including the face. I have seen two cases in which the profuse eruption so strongly resembled that of typhus fever that the diagnosis remained doubtful for two or three days. Murchison states that he has often succeeded in finding the spots on the back when they existed nowhere else, and he occasionally noted that they were larger and more numerous on the back than in front. This circumstance he attributed to the greater warmth of the skin of the back, on which the patient lies. Sometimes the eruption becomes more profuse after a warm bath, similar to what is often observed in measles and other eruptive fevers.

The spots usually appear first on the seventh or eighth day of the disease, sometimes not until the twelfth day. In rare instances they have been noted on the fifth day, and in children even as early as the fourth day of the disease. In three of Murchison's cases they did not appear until the fourteenth day and in one case not before the twentieth day.

The duration of the eruption varies greatly in different cases. The usual duration is about two weeks in cases of average severity. In cases of long duration or attended with relapses the spots may continue to appear as late as the fifth week after their first appearance. In children the eruption rarely lasts longer than seven or eight days. As a rule, the eruption disappears with the beginning of convalescence, but Murchison makes the important observation that in

some cases the spots continue to come out when the general symptoms have begun to improve and the patient is apparently convalescent. As long as the eruption continues a slight imprudence may cause a return of the fever.

Occasionally no eruption whatever is to be found, even on careful and repeated search. From an analysis of the figures of various observers it appears that the eruption is absent throughout the disease in about twenty per cent. of all cases. It is most frequently present in cases between the ages of ten and thirty years, being absent in only ten per cent. In cases under the age of ten, the eruption was not found in about twenty-two per cent., nearly one in four. In cases over the age of thirty it was absent in sixteen per cent. Pepper believes that there is a great difference in the amount of the eruption in different epidemics and in different seasons. Murchison holds that there is no relation, as in typhus fever, between the severity of the disease and the abundance of the eruption. It is the general opinion of other writers that a copious eruption is a favorable sign rather than otherwise. In fatal cases the eruption is more frequently absent or poorly developed than in those which recover.

There is some difference of opinion as to whether the rose-colored eruption is ever found in diseases other than typhoid fever. A few observers have stated that they have met the lenticular spots in cases of other acute diseases, particularly acute phthisis. The best authorities, however, including Louis and Murchison, agree that the typical rose-colored eruption is peculiar to typhoid fever.

Accidental Eruptions.

There are various accidental eruptions which are often seen in typhoid fever. They have no symptomatic or diagnostic significance as they are not peculiar to the disease, but they nevertheless call for some description.

Erythema or Scarlet Rash.—In some cases of typhoid fever the rose-colored eruption is preceded for a day or two by a diffuse erythema, which may cover the entire body. When it occurs in association with sore throat it is sometimes mistaken for scarlet fever. It may persist throughout the fever, according to Murchison. This erythema is not confined to typhoid fever, but is seen in other diseases.

Purpura spots and vibices are occasionally met with, occurring independently of the rose sports. They are said to be most common in patients of a hemorrhagic diathesis.

Taches-bleuâtres.—Spots of a pale blue color and of varying size and form are occasionally observed upon the skin in typhoid fever. The French have given them the name of taches bleuâtres. They

are not elevated above the skin and do not disappear on pressure. They often follow the course of the small subcutaneous veins and are most commonly found on the abdomen, back, and thighs. They are met with in other diseases and are believed to be caused by *pediculi.*

Sudamina.—Sudamina occur not infrequently in typhoid fever. Murchison found them in one-third of his cases. The vesicles are very minute and generally discrete. They may be found on every part of the body except the face, but their usual seat is the anterior and lateral surfaces of the chest and abdomen. They first appear in the second or third week of the disease and are most common in cases attended with profuse sweating. They are generally followed by desquamation of the cuticle of the parts of the body most affected. Sudamina were thought by Louis to have a specific character in typhoid fever, but it is now generally admitted that they are equally common in all febrile diseases attended with sweating.

Desquamation in fine branny scales may occur in typhoid fever independently of the development of sudamina. It sometimes follows the scarlet rash above described when the erythema has been very pronounced or extensive, or it may occur without obvious cause. The hair often falls out during convalescence and the nails present atrophic markings such as are seen in other acute diseases.

Circulatory System.

The Blood.—The changes in the blood in typhoid fever have been carefully studied by many observers and their conclusions are in substantial agreement. At the beginning of the fever the red corpuscles are generally normal in number, and often at the upper limit of normal as the patients are usually young and healthy individuals. Profuse sweats or diarrhœa at this period may even cause concentration of the blood. Cold baths have a like effect, if the blood is examined just after the immersion. During the height of the fever there is generally a gradual though slight fall in the number of red cells, which becomes more marked at the end of the febrile stage and extends into the beginning of convalescence. The lowest point is reached about the first week of convalescence, the number then gradually rising to normal. As a rule, the fall in the number of red corpuscles bears a direct relation to the severity of the case, but occasionally a grave anæmia may follow a mild case of the disease. Chart No. 5 is from an instance of this kind described by Thayer, in which the anæmia was extreme, although the symptoms at no time were alarming and the temperature reached a normal point on the twentieth day. This chart has been referred to by some recent writers as if it represented

the ordinary anæmia of typhoid fever, although Thayer expressly states that the anæmia is generally slight. Even very severe and fatal cases show as a rule a relatively slight anæmia. This is well illustrated in the following table constructed by him from cases in Osler's wards, where careful blood counts were made during the fever:

1st week.	2d week.	3d week.
2 counts, 5,636,000.	10 counts, 4,960,599.	9 counts, 4,951,535.
4th week.	5th week.	6th week.
6 counts, 4,038,333.	7 counts, 3,856,786.	4 counts, 4,364,250.

Later counts show a gradual increase.

The hæmoglobin diminishes with the red cells, but usually to a greater extent and it rises more slowly to the normal standard. In the case above referred to, the percentage of hæmoglobin fell to 20, at the time the red corpuscles numbered 1,352,000 to the cubic millimetre.

The following table shows the average percentage from week to week, in twenty cases in Bellevue Hospital:

1st week.	2d week.	3d week.	4th week.	5th week.	6th week.	7th week.	8th week.
92.5	84.3	76.8	69.	51.	66.5	....	86.

In order to show the moderate grade of anæmia that usually prevails in typhoid fever I have constructed Chart No. 6, using for the purpose the blood counts given by Thayer, combined with the results obtained in twenty-two cases in Bellevue Hospital.

The number of leucocytes in the cubic millimetre is about normal at the beginning of the fever, but tends to diminish throughout the course, reaching the lowest point towards the end of defervescence. During convalescence the number increases again and reaches the normal in six or seven weeks. These changes are shown in the following table given by Thayer:

1st week.	2d week.	3d week.
21 counts, 6,984.	50 counts, 6,468.	40 counts, 6,260.
4th week.	5th week.	6th week.
28 counts, 5,877.	16 counts, 6,621.	5 counts, 7,000.

Thayer adds that these figures are not so low as those given by some authors, but they show clearly the absence of leucocytosis and the tendency towards a slight progressive diminution in the number of leucocytes during the progress of the disease. The absence of leucocytosis in uncomplicated typhoid fever is the most important feature. When an inflammatory complication occurs the white cells are at once markedly increased. Cold baths are also followed by a decided temporary increase in the number of leucocytes.

The qualitative changes in the leucocytes are of importance. The multinuclear elements progressively diminish with a corresponding

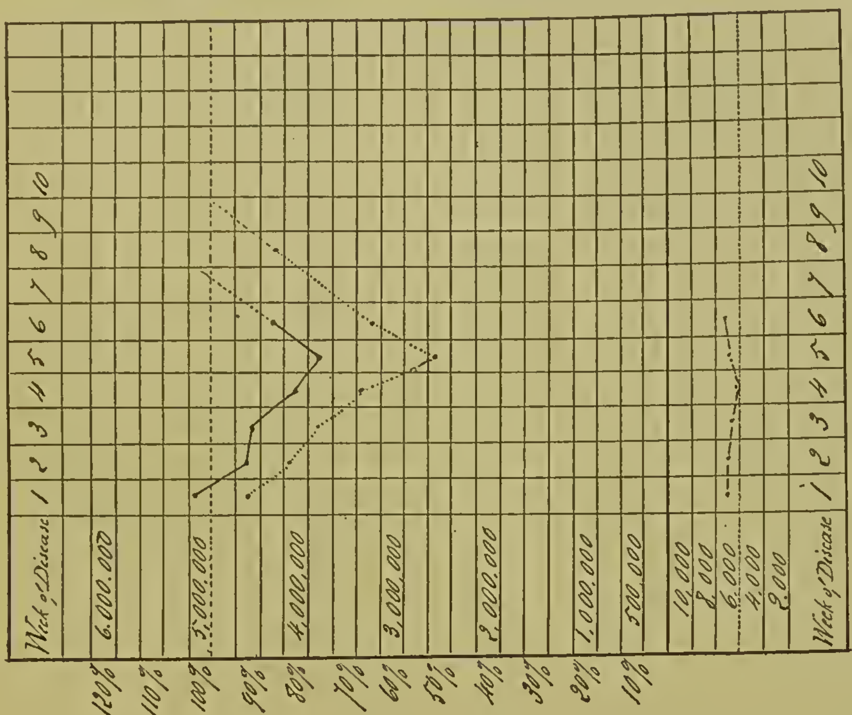

CHART No. 6.—Showing the Ordinary Anæmia of Typhoid Fever. Continuous line, red corpuscles; dotted line, hæmoglobin; broken line, white corpuscles.

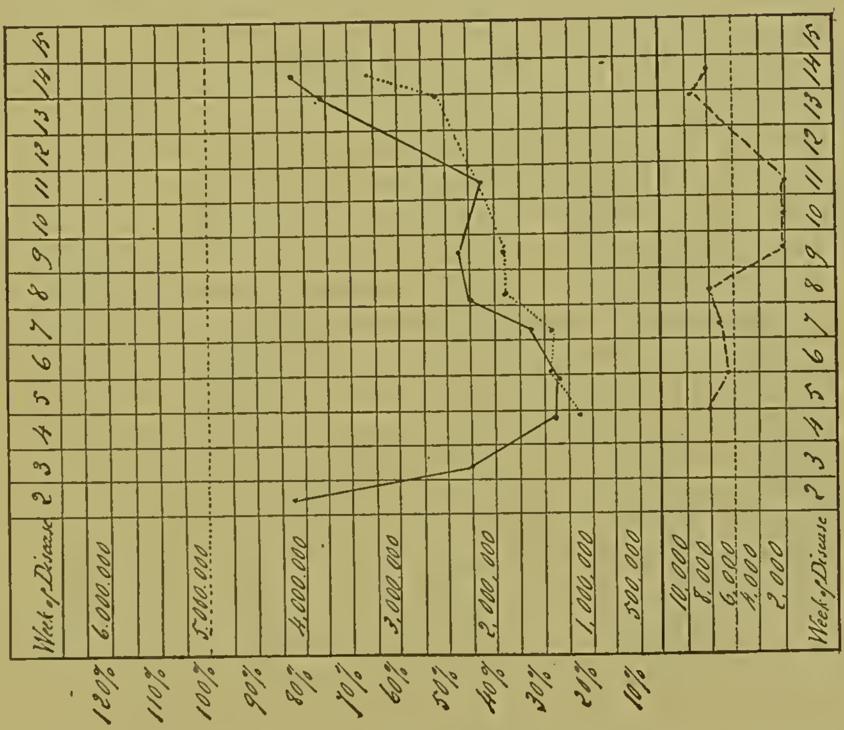

CHART No. 5.—Showing Extreme Anæmia Occasionally Observed in Typhoid Fever. Continuous line, red corpuscles; dotted line, hæmoglobin; broken line, white corpuscles. (Thayer.)

increase in the large mononuclear leucocytes. This condition may not be well marked in the first or second weeks, but becomes more

so as the fever continues. It is not until after the disappearance of fever that the multinuclear cells begin to increase again and their normal percentage is not reached until the tenth or eleventh week. According to Thayer, these changes in the proportion of the different varieties of leucocytes are very characteristic and serve to distinguish the blood of typhoid fever from that of most of the other febrile processes with which it is likely to be confounded. A majority of these conditions are inflammatory in nature, and all show at least a normal, and usually a considerably increased number of multinuclear cells.

The *pulse* is accelerated in typhoid fever. The rate generally varies with the temperature curve, falling in the morning and rising in the evening. The absolute frequency of the pulse, however, is less than in most diseases characterized by high temperature. The usual rate in cases of moderate severity is from 90 to 110 per minute. A very rapid pulse indicates, as a rule, that the case is severe, and the prognosis is always doubtful when the rate is persistently more than 120. The pulse is subject to great variations in the same individual on different days and even at different hours on the same day. The pulse and temperature do not always correspond, and it is not very uncommon to see a pulse of 100 with a temperature of 104° or more. In some cases the pulse may even remain within normal limits throughout the disease, though there may be several degrees of fever. Murchison has reported several cases in which the pulse was subnormal throughout the fever, rising to normal figures in convalescence. Liebermeister believes that the comparative slowness of the pulse in typhoid fever is due to the depressing influence of the toxæmia. On the other hand, in some cases of afebrile typhoid, as in one case under my observation, the pulse may be abnormally frequent and serve as the chief indication of the toxic condition of the patient. In other cases of afebrile typhoid the pulse is normal. It is evident, therefore, that there are other agencies besides the temperature which influence the frequency of the pulse. The condition of the heart muscle is probably a most important factor in this disease as in others in determining the rate as well as the quality of the pulse.

Apart from the general quickening of the pulse, temporary accelerations may occur at any time from slight causes. This is especially true towards the end of a severe and protracted case when both pulse and temperature are in a state of unstable equilibrium. Slight emotional excitement, the visit of a friend, a change of position in bed, or a meal of solid food, may cause a decided increase of the pulse rate during convalescence even though the attack has been of only moderate severity. The occurrence of a complication, such as

intestinal hemorrhage or perforation, usually has a marked quickening effect upon the pulse.

The quality of the pulse varies considerably at different periods in typhoid fever. With the onset of the disease the pulse is full and strong, at all events in well-nourished individuals. Early in the second week there is usually a marked change and the pulse is soft and compressible and generally becomes dicrotic. This dicrotism is regarded by many observers as peculiar to typhoid fever. It is not limited to this disease, but is also found in other febrile diseases in which there is diminished arterial tension. It is seldom, however, that the phenomenon is so well marked as in typhoid fever, and in doubtful cases it is often of service in establishing the diagnosis. Irregularity or intermission of the pulse is rare, but is occasionally noted in severe cases. It is a very unfavorable symptom, but recovery sometimes occurs. The systolic impulse of the heart usually becomes very feeble and often cannot be felt at all. At the same time, the first sound may become inaudible, while the second sound continues to be heard. A soft, blowing murmur at the apex may accompany or take the place of the first sound of the heart.

Respiratory System.

The *respiration* in typhoid fever is somewhat quickened, even in the absence of pulmonary complications. It varies generally, but not always, directly with the pulse. The rate in a case of moderate severity is usually from 24 to 28 a minute. In severe cases the respiratory movements may reach 36 to 40, though there may be only a slight bronchitis present, or no pulmonary lesion whatever. The rate is always more rapid than normal, even in those cases of afebrile typhoid in which both pulse and temperature remain within normal limits throughout the disease.

Bronchitis, of greater or less severity, is so constantly found in typhoid fever that it is to be regarded as a symptom rather than as a complication of the disease. As a rule, the physical signs are limited to sibilant and sonorous râles heard here and there in the chest, and the patient may not be conscious of any embarrassment of his respiratory functions. In other cases the bronchial catarrh may extend into the smaller tubes and harassing cough and perhaps urgent dyspnœa may be the most prominent symptoms in the disease. The frequency of bronchitis seems to vary greatly in different years and in different epidemics. Murchison noted it in only twenty-one out of one hundred cases, but in the experience of American physicians, some signs of bronchitis are found in all but a small minority of cases.

Digestive System.

Anorexia, more or less complete, is a constant symptom of typhoid fever, except in very mild cases. It is also one of the earliest symptoms, being usually well marked when the patient first comes under observation. As the fever declines the appetite returns and the patient clamors for food. Thirst is usually present early in the attack but becomes less marked as the disease progresses.

Nausea and vomiting are not very uncommon at the beginning of the illness and the patient may be regarded at first as suffering from a simple "bilious attack." Murchison noted vomiting in 36 out of 100 cases. In my own experience it was mentioned in 44 of 143 cases, or in 30.8 per cent. Of the 143 cases, 22 were children under fifteen years of age, in whom vomiting is said to be more common than in adults. In this particular series of cases, however, it was less frequently reported in the children than in the adult cases. Generally, the vomiting ceases with the progress of the disease, probably because of the careful and restricted diet of the patient. In rare cases the vomiting is persistent and may be difficult to control. Murchison regarded vomiting as a favorable symptom when it occurred at the commencement of the illness. Later in the disease, however, it may be the first symptom of peritonitis. Pain and tenderness in the epigastrium, with or without vomiting, are often present in the early stages, but they are seldom symptoms of great urgency.

The *tongue* at the beginning of the attack is moist and coated with a white, pasty fur, with the exception of the margins and tip which are bright red. As the disease progresses the coating usually disappears, and in mild cases the tongue may be clean and moist throughout the illness. In severe cases the tongue becomes dry and it may be covered with a thick brown crust. In other cases it may remain clean but is red, dry, smooth, and glazed in appearance. In unfavorable cases, especially when protracted, deep transverse fissures may form on the surface of the tongue. All these conditions may be much modified by careful attention to the tongue from the beginning of the disease. A moist tongue is usually considered a favorable indication, but Murchison and other writers have reported fatal cases in which the tongue never became dry and brown, but remained moist throughout the illness

The *lips* are generally dry and often become cracked and fissured and bleed easily. In severe cases, sordes collects on the teeth, calling for frequent cleansing. The dryness of the lips and tongue is favored by the tendency of the patients to breathe through the mouth. Some-

times stomatitis may occur, with the formation of ulcerations upon the tongue and the buccal mucous membrane. The gums also may become spongy and give rise to hemorrhage.

Tympanites is present in most cases of typhoid fever. It is sometimes observed early in the disease, but generally not until the second week. The gaseous distention is most marked in severe cases, especially those in which there is diarrhœa. Murchison noted tympanites in 79 out of 100 cases. In 17 the distention was extreme and in 7 of these death occurred, whereas of 21 cases in which there was no tympanites, none was fatal. Louis noticed great meteorism in one-half of his fatal cases, but in only 7 of 88 cases which recovered. It is evident, therefore, that tympanites is always a serious symptom, while its absence is a favorable indication. I have, however, records of several very severe cases in which the symptom was absent throughout the disease. Two of these cases ended fatally, one after profuse intestinal hemorrhage.

Tenderness on pressure in the right iliac region is a common symptom in typhoid fever. If diarrhœa is present a sensation of gurgling may also be felt by the hand on pressure in the same region. The tenderness is a symptom of considerable diagnostic value, as it is in all probability due to ulceration in the intestine and is rarely found in other conditions. It is, however, often absent in well-marked cases of the disease. In former times, much significance was attached to the sensation of gurgling in the iliac fossa, particularly by Chomel, who believed that it is much more common in typhoid fever than in ordinary diarrhœa. The symptom is due simply to the presence of fluid fæces and gas in the bowel, and it can be found, if sought for, in almost every case of severe diarrhœa and often even in health. Most modern observers, therefore, hold that its presence or absence is a matter of little importance.

Enlargement of the spleen is a most constant feature of typhoid fever as of other acute infectious processes. It can usually be detected by palpation, if the case be seen sufficiently early. The most favorable time for the demonstration of the splenic enlargement is at the end of the first week or during the first part of the second week, as tympanites has not usually developed at that early period. In cases free from gaseous distention of the abdomen the spleen may be palpable throughout the disease. Some observers depend upon percussion as a means of determining the size of the spleen in typhoid fever. In my experience this method of exploration gives less satisfactory results than palpation in this disease, though I am accustomed to employ both methods in every case. Very moderate tympanites will often mask a splenic tumor, if reliance be placed upon

percussion, whereas the organ may be felt by the finger tips with a little manipulation of the patient. According to Murchison the enlargement is greatest in persons under thirty years of age. It is said to be often absent in elderly typhoid patients. I have repeatedly failed to detect it in children, particularly in mild cases.

Diarrhœa is a frequent symptom of typhoid fever. At the beginning of the attack there is often constipation which, as the disease develops, changes to diarrhœa, either spontaneously or as the result of a purgative. In a large proportion of cases, however, the bowels remain constipated throughout the illness. Of my own cases, particularly in private practice, fully one-third have constantly required laxatives or enemata. In other cases, the movements have been almost as regular and as fully formed as in health. When diarrhœa exists, it varies greatly in intensity. In the majority of cases, the number of stools does not exceed two to four in the course of the day. In severe cases, the number may reach twelve or even twenty in the twenty-four hours. A moderate diarrhœa does not appear to add to the gravity of a case. In fact, patients seem to do better with two or three rather loose movements a day than if the bowels are confined or moved only once in two or three days. A profuse and persistent diarrhœa, on the other hand, is very unfavorable, and if unchecked may cause death by exhaustion. The diarrhœa is not due to the intestinal ulcerations, but is caused by the associated catarrh of the bowels, and the severity of the diarrhœa bears no relation to the extent of the local lesions. It is impossible, therefore, to accept without some reservation the opinion of Murchison that "the severity and danger of the disease are in direct proportion to the severity of the diarrhœa." All observers have repeatedly seen profuse intestinal hemorrhage or perforation occur in cases in which there had been no diarrhœa whatever. Chart No. 4 is from a case in which a severe hemorrhage occurred on the ninth day, though the bowels had been constipated and remained so throughout the disease. Extensive lesions are also often found after death in cases in which previously there had been neither diarrhœa nor any other abdominal symptom. Murchison cites an instructive case mentioned by Wilks of a girl who died at the end of the third week; her bowels had been confined, and after death the small intestines were found filled with small scybala, with an ulcer beneath each.

Diarrhœa may begin at any period of the disease and its duration varies in different cases. It may be one of the earliest symptoms in the onset and may cease shortly after the patient comes under observation and treatment, or it may continue throughout the illness. In other cases it may not occur until the second or third week, or even

later in the disease when convalescence has apparently begun. Murchison has seen cases of relapse in which the bowels were constipated during the primary attack and loose in the relapse.

The *characteristic stools* of typhoid fever are light yellow in color. They are usually liquid and often resemble pea soup in color and consistence. Their reaction is alkaline and the odor very offensive and ammoniacal. Upon standing they separate into an upper cloudy liquid layer and a lower layer composed of flocculent yellow masses. The sediment contains crystals of triple phosphate which are of no significance, except as evidence of decomposition. The decomposition and the yellow color of the stools are probably both the result of the diminished secretion of bile by the liver. When the bowels are regular or constipated, the stools are generally of a darker yellow and are fully formed or semisolid in consistence.

Typhoid bacilli are generally present in the stools of typhoid patients throughout the febrile stage of the disease. Bacteriologists have long sought for a means of isolating and identifying in pure culture the typhoid bacilli from the stools and urine of patients suffering from typhoid fever. Various methods have been proposed, but they have not proved practical or certain in their application. Hiss, however, of the New York Health Department, has recently devised a method by which he is able to recover and identify the typhoid bacilli within less than forty-eight hours, from speciments of fæces and urine containing them. This method was tested on the fæces in 19 cases, and in 17, or 89.5 per cent., he succeeded in isolating the bacilli. The bacilli were found as early as the sixth day and as late as the thirtieth day, and in a case of relapse on the forty-seventh day of the disease. The bacilli seem to be more numerous in the stools from the tenth or twelfth day of the fever. The convalescent cases gave uniformly negative results.

Intestinal hemorrhage is a rather infrequent symptom in typhoid fever. Its frequency apparently varies considerably with different observers and in different epidemics under the same observers. Of 1,564 cases under the care of Murchison copious hemorrhage (over six ounces) occurred in only 58, or 3.77 per cent. Strümpell states that he saw in his clinic at Leipsic in the course of several years 45 intestinal hemorrhages in 472 cases, that is, in 9.5 per cent. In one year (1880) the percentage rose to 18. Liebermeister noted hemorrhage in 127 out of 1,743 cases, or in 7.3 per cent. It is probable that Strümpell and Liebermeister included slighter forms of hemorrhage than did Murchison in his estimates. On collating the experience of various observers it appears that hemorrhage from the bowels took place in 277 out of 4,594 cases, or in just 6 per cent.

Intestinal hemorrhage occurs most often in severe cases. It is natural, therefore, that its frequency should vary in different epidemics according to the type of the disease. It is, however, sometimes observed in mild cases. In nearly one-third of Murchison's cases, 18 out of 60, the symptoms had been mild up to the occurrence of the hemorrhage. According to Liebermeister the bleeding occurs twice as often in women as in men, in 10 per cent. of the cases in the former, and in only 5 per cent. in the latter. It is a very rare occurrence in children, the proportion being less than 1 per cent. Here again, however, the experience of some observers differs from that of others. Meigs and Pepper speak of hemorrhage as comparatively frequent in children, stating that Hillier observed it 4 times out of 30 in which the stools were carefully examined. On the other hand, in 252 patients under fifteen years of age observed by Taupin, and Rilliet and Barthez it occurred only once. The frequency of the accident increases with the age of the child. Of 946 cases collected by Holt, mainly from hospital reports, hemorrhage occurred in 30, or about 3 per cent.; but the majority of these were in children over ten years old. Morse also reports that in 77 children under ten years of age there was no case of hemorrhage; while in 204 between ten and fifteen years it was seen in 9 cases. When we consider the mildness of the disease in children, and the slight extent of the lesions in the intestine, it would be surprising if hemorrhage were not a rare event in the typhoid fever of childhood. It is probable, however, that the bleeding passes unnoticed in some cases because of the absence of clinical symptoms calling attention to it.

The hemorrhage occurs most frequently towards the end of the second week or in the third or fourth week of the disease. Occasionally bleeding may take place early in the disease, but in such cases it is usually slight in amount. Of 59 cases observed by Murchison, in which the date was noted, the hemorrhage began during the second week (mostly towards its close) in 8; during the third week in 28, during the fourth in 17, during the fifth in 1, during the sixth in 3, during the seventh in 1, and during the eighth week in 1. In the cases observed by Liebermeister, the bleeding took place, as a rule, at an earlier period. Of 81 cases the hemorrhage occurred during the first week in 7, during the second week in 33, during the third in 19, during the fourth in 14, and in 8 at a later period. As already suggested, Liebermeister probably included in his cases the lighter hemorrhages which occur early in the disease.

The amount of blood lost may vary from a mere trace to several pints. It is usually fluid and bright red in color. If it is retained for some time in the bowels it is passed in clots of a dark-red or

dark-green color. In some cases the amount is so small and so intimately mixed with the fecal matter as to be very difficult of recognition. In other cases a quart or more may be passed at one time. Murchison has seen cases of extensive hemorrhage in which the patients have died within a few hours of its occurrence before any blood has been voided externally.

The source of the bleeding varies at the different periods of the disease. The early and slighter hemorrhages are usually due to rupture of the capillary vessels of the congested mucous membrane of the intestine. Sometimes they are due to a general dyscrasia of the blood and are then associated with hemorrhages in other parts of the body. The bleeding later in the disease generally comes from a small artery which has been laid open by intestinal ulceration or by the separation of a slough from a Peyerian gland. The quantity of blood lost in such cases is usually very large. Occasionally, however, profuse hemorrhages have occurred so early in the disease that intestinal ulceration had probably not taken place. Murchison refers to several such cases. Chomel also mentions cases in which blood was found in the intestines before ulceration had begun.

The symptoms of intestinal hemorrhage depend upon the amount of blood lost. If the quantity is small there may be no effect whatever upon the patient and the bleeding may pass unnoticed until the blood appears in the stools. If the amount be considerable it is indicated by an abrupt and decided fall of the temperature, associated with an accelerated pulse and with pallor of the face and increased prostration. (Chart No. 4.) The lowering of the temperature is only temporary; it soon rises to its former height or to a still higher level. The more extensive the hemorrhage, the more marked the signs of collapse of the patient. There may be syncope or vertigo with tinnitus aurium, and cold extremities. As a rule, the patient recovers from the immediate effects of the bleeding. Occasionally, however, as stated above, the case may terminate fatally within a few hours. Trousseau, indeed, has seen death follow in less than one hour after first signs of the hemorrhage.

Intestinal hemorrhage should always be regarded as a serious symptom, though its gravity is not the same in all cases. When it is slight and occurs early in the disease, it is possible that it may do good by relieving intestinal congestion. Such good effect, however, is probably only temporary and has no influence upon the general result of the case. A slight bleeding also may be the precursor of others that are more severe. Occasionally, however, the hemorrhage is succeeded by a marked improvement in the general condition of the patient. The nervous symptoms abate, delirium subsides, and

the brain clears. In some instances the improvement is permanent, and convalescence is established. The occasional occurrence of such cases has led some observers, particularly Graves and Trousseau, to speak of intestinal hemorrhage as a rather favorable symptom. Graves simply states that he has seen certain cases in which the hemorrhage was thought to be productive of marked benefit. Trousseau takes much stronger ground. As a result of long observation and study of the question, he is of the opinion that intestinal hemorrhage in typhoid fever, instead of being of the gravity that is usually assigned to it, is most frequently a symptom of favorable import. These views, however, are opposed by the large majority of writers and common experience is against them. Of 60 patients observed by Murchison, 32 died; in 11 of the 32 cases the immediate cause of death was peritonitis; death occurred in 14 of the remaining cases within three days of the bleeding, and in 8 of the 14 within a few hours. It is true that Murchison included in his estimates only cases of copious hemorrhage. But the mortality reported by other observers is also high, over one-third of the cases terminating fatally. Of 282 (adult) cases that I have collected from various sources, 122, or 42.8 per cent., proved fatal. The mortality is about the same in children. Montmollin reports 14 cases with 4 deaths and Morse 9 cases with 5 deaths. Murchison is of the opinion that profuse hemorrhage is always a formidable symptom. He writes that although he has "known many patients recover, he has never observed benefit from the occurrence," and he has "repeatedly seen patients die unexpectedly by syncope a few hours after a copious bleeding, who had previously done well. Moreover, when the patient survives the effect of the bleeding, there is an unusual risk of his dying of peritonitis. The bleeding makes it probable that the ulceration has extended to the vessels beneath the transverse muscular fibres, and such ulceration is not unlikely to go on to perforation." Trousseau's view of the significance of intestinal hemorrhage was probably in large part due to his conception of the pathology of the occurrence. He did not believe that the hemorrhage was dependent upon the ulceration in the bowel. He considered that the blood, as a rule, simply transuded from the congested mucous surface, as in ordinary epistaxis or hæmatemesis. If, then, the loss of blood was not in itself sufficient to cause death, he had no fear of evil consequences from the lesion underlying the hemorrhage. This conception of Trousseau's is not accepted by others, except, as we have seen, for the slighter forms of bleeding, such as occur early in the disease. Liebermeister discusses at some length the opinions of Graves and Trousseau in an endeavor to understand how observers of such extensive experience could have

arrived at conclusions so much at variance with those generally received. He is ready to admit that these hemorrhages have not so dangerous a significance as was formerly thought, and is still believed by the laity. It is rare, he says, that a patient dies as the direct result of the hemorrhage, or during the collapse that immediately follows it. Of his one hundred and twenty-seven patients, seventy-eight, or by far the greater number, recovered. The improvement of symptoms that sometimes follows a hemorrhage must also be taken into account. Liebermeister holds further that the statistical evidence of the gravity of the symptom is not quite so conclusive as it at first sight appears; for intestinal hemorrhages occur most frequently in the severest cases of the disease, in which the mortality without hemorrhage would still be the highest. In some fatal cases, he continues, the hemorrhage is in no way responsible for the result; in many others, however, it apparently contributes to the production of cardiac paralysis. While, therefore, intestinal hemorrhage must be regarded, on the whole, as affecting the prognosis unfavorably, yet each individual case is to be judged on its merits. A slight discharge of blood, in a case already recognized as grave, adds nothing to its gravity, except in so far as it excites the fear of a more copious return of the same. This reasoning of Liebermeister seems rather to beg the question. If the hemorrhage, as a general rule, occurs in the most severe cases of typhoid fever, it furnishes additional evidence of their gravity. It cannot then be considered a favorable symptom in such cases, for Liebermeister agrees with Murchison and clinicians generally in attributing all considerable hemorrhages to the intestinal sloughing and ulceration. The bleeding, in fact, is sometimes the first positive symptom that the intestine is deeply involved.

It is sometimes asserted that intestinal hemorrhage has become more frequent since the introduction of the cold-bath treatment of typhoid fever. It is argued that the anæmia of the skin produced by the cold water must cause a determination of blood to the internal organs, including the bowels, and thus favor hemorrhage. Liebermeister's experience goes to prove that the contrary is the case, namely, that the hemorrhages have diminished in frequency under the cold-water treatment. Of 861 cases under his care before the introduction of this mode of treatment in 72, or 8.4 per cent., there was hemorrhage, whereas of 882 cases treated since the introduction of cold baths, hemorrhage occurred in only 55, or 6.2 per cent. Nevertheless, practitioners are agreed that when intestinal hemorrhage does occur it constitutes a contraindication to the use of cold baths.

Nervous System.

The symptoms of derangement of the nervous system are among the most important as well as the most constant of the clinical phenomena of typhoid fever. Although the specific anatomical lesions of the disease are situated in the intestinal tract, many a case will run its course without a single symptom referable to the abdominal organs. Instances have even been reported in which the intestinal changes have themselves been wanting, although the cases resulted fatally. The nervous symptoms, on the other hand, are always present, to a greater or less extent, even in the mildest cases. Hence the term "nervous fever" so much employed by the old writers. It was formerly generally believed, and maintained especially by Liebermeister, that these symptoms were caused by the prolonged high temperature. Under this view it was difficult to explain their presence in cases in which the pyrexia is very moderate or even wholly absent, and in many of these cases characterized by a low temperature the nervous disturbances are very marked. The bacteriological researches of the last fifteen years, to which we are indebted for a correct understanding of the etiology of typhoid fever, have also furnished us with a clear explanation of the nervous symptoms. It is the specific infection of the disease, the toxæmia, which is the cause of the derangements of function of the nervous system. Prolonged high temperature may also be a factor in their production, but it is not an essential one. In considering the various symptoms of nervous disturbance I shall take them as far as possible in the order of their occurrence in the disease.

Headache is one of the most constant as well as one of the earliest symptoms of typhoid fever. Murchison noted it in 77 out of 82 cases and Louis found it in all but 7 out of 133 cases. In my own experience it is even more common, being present in all but 5 out of 143 cases in which its presence or absence was ascertained. In many cases it is the first symptom of which the patient complains and the one which gives him the most concern during the prodromal period of the disease. It continues through the stage of invasion, often with increasing intensity, but usually subsides with the full development of the fever. It is usually referred to the forehead, but sometimes affects the occipital region, or it may be generally distributed over the entire head, with hyperæsthesia of the scalp. The pain is usually described as dull and heavy, but sometimes it is very severe and may be paroxysmal or neuralgic in character. Headache is probably as frequent in children as in adults.

Dizziness or *vertigo* is not infrequent during the period of incubation and even later in the disease. It is recorded in about one-tenth of my cases. It is not noted during the height of the fever, but sometimes manifests itself again at the beginning of convalescence.

Pains in the back and extremities are present at the beginning of the disease, in almost all cases. The pains are especially severe in the thighs and legs. There is also often a general aching of the whole body, with a sensation of extreme weariness. These symptoms do not differ, except perhaps in degree of severity, from those observed in other acute infectious diseases. In some cases the pain is localized in the back of the neck. I have seen one striking instance of this, in a boy eight years of age, who apparently suffered the most intense pain in the region of the cervical vertebræ on the slightest motion of the head. The rachialgia may also be severe in the dorsal region and may be accompanied with neuralgic pains in the legs. At times, the pain is situated in the joints and the case is at first mistaken for one of acute articular rheumatism, the "arthro-typhoid" of some writers.

Wakefulness is a common symptom in typhoid fever from the beginning of the disease. The sleep is restless and disturbed by dreams. The wakefulness is sometimes very distressing and difficult to combat. It rarely lasts more than eight or ten days and is then usually succeeded by drowsiness. In exceptional cases the patient may remain wakeful until convalescence is established.

Somnolence, more or less marked, is rarely absent in typhoid fever. It usually appears in the course of the second week. Occasionally, especially in severe cases, it is observed at an earlier period, even as early as the first day. In some cases, it is limited to a certain degree of listlessness or apathy. The somnolence is usually slight at first, but increases rapidly as the disease progresses, particularly in severe cases. In fatal cases, it usually continues without interruption until death takes place. In general, its duration varies directly with the intensity of the typhoid infection. It often alternates with delirium, the patient being restless and delirious at night, but heavy and somnolent during the day. The somnolence may deepen into complete unconsciousness. This was noted by Murchison in twenty-two of his one hundred cases. Somnolence is generally well marked in children and may make its appearance at the outset of the disease.

Delirium.—Delirium is present in a majority of cases of typhoid fever. In Murchison's series of 100 cases it was absent in only 33. Other observers have found this symptom less frequent. In my

own experience fully one-half of the patients passed through the attack without any delirium whatever. Probably the cold-bath treatment to which most of them were subjected helped to keep the mental faculties unimpaired. The frequency and severity of the delirium vary with the intensity of the infection, though its absence does not always indicate a favorable termination of the disease. Of Murchison's 33 cases in which there was no delirium, death occurred in 3, whereas of the other 67 cases, 18 were fatal.

The delirium usually makes its appearance in the course of the second week, but sometimes not until the end of the third week, or even later, during the period of convalescence. In rare cases it occurs much earlier. Louis observed it twice on the first day of the disease. Other writers have described cases in which active delirium was the earliest symptom noted. Murchison was consulted in three cases in which the disease was at first regarded as acute mania. In a case reported by Motet the patient had been taken to an insane asylum before the real nature of the illness was discovered. The pyrexia and its attending symptoms should put us on our guard in such cases.

The delirium varies in type and severity in different cases. When it appears at the onset of the disease, it is violent and maniacal in character, and may lead to errors in diagnosis, as in the cases referred to above. Usually, however, the delirium comes on more gradually, and generally appears first at night. It may be limited in the beginning to a slight confusion of thought or incoherence of speech and may be absent altogether during the day. In mild cases it often does not go beyond this stage. In severe cases, it increases with the other symptoms and may develop into a state of wild excitement. The patient sometimes breaks out into paroxysms of shouting and screaming and is with difficulty restrained in bed. If not constantly watched, he may throw himself out of the window. The more active and noisy the delirium the greater the danger, according to Murchison. Of eighteen cases in which he noted active delirium, nine ended fatally. In some cases the condition resembles delirium tremens, especially in individuals who have been intemperate. More frequently the delirium is of a low, muttering form—the typhomania of the older writers. The various forms of delirium may be present in the same patient. The active, noisy variety is especially apt to pass into typhomania as the prostration of the patient increases. This quiet form of delirium may pass on into a state of unconsciousness, a very unfavorable symptom. In only twenty-two of Murchison's cases was there at any time complete unconsciousness—in eleven of these cases death occurred. As already stated, the delirium is espe-

cially apt to occur at night, and it is often entirely absent during the day, even in severe cases. The delusions from which the patients suffer are generally connected with some event in their past life.

Delirium is less frequent in children than in adults, occurring in about one-third of the cases. It is usually mild and transient in character. The active form of delirium is rarely seen in children.

Prostration.—There is always more or less muscular prostration in typhoid fever. It is often slight in the beginning, but usually increases as the disease progresses. According to Murchison a large proportion of patients (forty-four out of one hundred of his cases) are able to sit up in bed and to get up to stool throughout the attack. Occasionally, in mild cases, patients are not confined to bed at all during the disease. Even in fatal cases there is sometimes but little prostration. As a rule, however, patients take to their bed early in the second week, and by the third week muscular prostration is marked and in severe cases the patient lies helpless upon his back unable even to turn from side to side. When the prostration is profound, there may be paralysis of the sphincters so that the urine and fæces are passed involuntarily. Occasionally there is retention of urine from paralysis of the bladder. There may be inability to protrude the tongue and also dysphagia.

Tremor.—Tremor is a constant symptom of the disease, even in the mildest cases. It is usually first noticeable in the tongue, when it is protruded for examination. The tremor is at first fine in character and may easily escape observation, but it becomes coarser and more evident with the increasing weakness of the patient. In severe cases the lips are tremulous, especially when the patient speaks. The hands also tremble when moved, and even when resting quietly upon the bed in cases of long duration. Tremor is observed in persons who are not addicted to the use of alcoholic liquors, but is naturally most marked in those who have been intemperate. Excessive tremor, not accompanied by other severe nervous symptoms, is indicative of deep ulceration of Peyer's patches, according to the experience of Murchison. Spasmodic twitching of the tendons of the wrist —*subsultus tendinum*—is observed only in severe cases and is a very unfavorable symptom. There are certain automatic movements which indicate a still more profound disturbance of tho nervous system. These are a constant picking at the bedclothes or at the lips or nose—*carphology*—or an aimless motion of the hands through the air. Protracted hiccough is sometimes observed late in severe cases and is aways of grave significance.

Muscular tremor is not frequent in children. Subsultus is occasionally observed, and also carphology, but both of these symptoms

are extremely rare, even in severe cases, according to most writers on diseases of children.

Muscular Spasm.—Spasmodic contraction of various groups of muscles is occasionally observed, even in mild cases. It is especially frequent at the very beginning of the disease. The muscles of the extremities are said to be most frequently affected, but those of the trunk and neck may also be involved. In one case of my own the earliest symptom was a most obstinate and painful wry-neck which persisted for some ten days. Sometimes there is spasmodic constriction of the pharynx so that the patient is unable to swallow. There may also be strabismus, or trismus, or spasm of the glottis. Murchison and other writers have recorded cases in which the head was so rigidly retracted that both deglutition and breathing were hindered, though most of the patients ultimately recovered.

Muscular rigidity is not often observed in children, but when it does occur it is a very grave symptom. Rilliet and Barthez observed it in five out of one hundred and seven cases, and all five cases terminated fatally.

Organs of Special Sense.

Organs of Vision.—The eyes in typhoid fever present nothing characteristic of the disease, except that the pupil is usually dilated, thus contrasting with the contracted pupil of typhus. The dilatation of the pupil is caused by partial paralysis of the sphincter muscle of the iris. There is also partial loss of accommodation from paresis of the ciliary muscle. These symptoms are due, according to Bull, to the general asthenic condition of the patient rather than to any lesion in the ciliary body or iris. Both occur during the height of the fever as well as during the period of convalescence. The eyes are usually dull and heavy in expression. There is sometimes haziness of vision, which is increased by sitting up. In addition to strabismus, which has already been mentioned, there is sometimes irregularity of the pupils. This latter symptom was observed by Murchison in six cases and would seem to indicate some affection of the meninges. In two of Murchison's cases, however, a post-mortem was made, and in neither case was any cerebral lesion whatever found to account for the state of the pupils. In cases in which there is profound stupor and complete unconsciousness, the pupils are often contracted, and Murchison has known them under such circumstances to be as contracted as in typhus. Some observers, especially Louis, have described cases in which the eyelids were firmly closed as if from intolerance of light. Louis has never known recovery to take place in a case presenting this symptom.

Organs of Hearing.—Ringing or buzzing noises in the ears are present in many cases in the early stage of the disease. They are said to be more marked and persistent in severe than in mild cases. Deafness is a very common symptom and may affect both ears or be limited to one. It usually comes on towards the end of the second week. When both ears are affected, the deafness is probably due to the blunted perceptions of the patient, or to catarrh of the Eustachian tubes, and is without especial significance. The patients almost uniformly recover and their hearing is unimpaired. Deafness of one ear is of more serious import, as it may be due to suppurative otitis which may extend to the meninges of the brain.

Hyperæsthesia of the skin is not a frequent symptom. Murchison noted it in about five per cent. of the patients under his care. He did not consider it of great importance. It is most common in women and children and may occur early in the disease or not until convalescence. The abdomen and lower extremities are most frequently affected. In some cases the skin is so sensitive that the slightest touch causes the most exquisite pain. In one case under my care it was almost impossible to take the pulse of the patient without causing her to wince or even to cry out. In this case there was multiple neuritis affecting both hands and feet. According to Murchison, tenderness over the spines of the cervical or dorsal vertebræ is usually present. The abdominal tenderness due to cutaneous hyperæsthesia must be carefully distinguished from that due to peritonitis.

Anæsthesia of the skin is occasionally observed. Rilliet and Barthez regard it as a grave symptom when it occurs in children.

The *sense of taste* is frequently much impaired. This is due partly to the blunted perception of taste and partly to the thick covering of the tongue and fauces.

Epistaxis is a common symptom, occurring in from one-fourth to one-half of the cases. It is so frequent in the experience of some observers that they regard it as of considerable diagnostic value. It usually occurs early in the disease, during the period of invasion, but it may occur at any stage. The amount of blood lost may vary from a few drops to several pints. Unless the hemorrhage is profuse it has but little permanent effect upon the course of the disease. Pepper has occasionally seen apparent temporary relief to severe headache and restlessness from a free epistaxis in the early stages of the fever. On the other hand, a profuse bleeding may be the immediate cause of death. Murchison has recorded several instances of death from epistaxis.

Genitourinary System.

The urine in typhoid fever presents the general characteristics common to the urine in all acute febrile diseases. During the first week or ten days the quantity is greatly diminished, the color is high, the reaction is strongly acid, and the specific gravity is much increased above the normal; in other words, we have the concentrated urine of fever. The daily quantity may fall to one-quarter or even one-sixth of the normal amount for twenty-four hours. It varies considerably in different cases, depending upon the height of the fever, the amount of fluid taken, the amount excreted, and the presence or absence of diarrhœa. As the disease progresses the quantity usually increases and generally reaches the normal standard by the third or fourth week, even though fever be still present. In some cases the diminution persists until convalescence. When convalescence is established the quantity is uniformly increased and usually becomes much greater than normal.

The strong acidity of the urine in the beginning is due to its concentration, not to an increased excretion of acid. In fact, the experiments of Parkes have shown that the amount of acid is actually less than in health. As the disease progresses, the urine loses its acid character and may even become alkaline.

The specific gravity is rarely below 1.020 in the early stages and is usually much above these figures. I have known it to be as high as 1.040 in one instance. With the increase in the quantity of the urine the specific gravity falls and may be as low as 1.005 in convalescence. Hewetson reports that in fifty cases in the Johns Hopkins Hospital the average specific gravity in the different weeks was as follows: 1.024 in the first, 1.022 in the second, 1.018 in the third, 1.019 in the fourth, 1.014 in the fifth, 1.016 in the sixth, and 1.013 in the seventh week. These cases were all treated with cold baths.

The daily excretion of urea is usually much increased, especially during the first week. In one instance A. Vogel found the amount to be 1,200 gr. in twenty-four hours. After the first week, the quantity decreases, but remains above the normal as long as there is fever. As a rule, there is a close correspondence between the temperature and the excretion of urea; the higher the temperature the greater the amount of urea. The occurrence of inflammatory complications, such as acute pleurisy, may reduce the amount of urea, even to a point below normal. It is not, however, influenced by the diarrhœa; hence, observes Murchison, the intestines cannot be regarded as a channel for the elimination of urea in typhoid fever. In convales-

cence, the quantity is often much below the normal. Some writers hold that the amount of urea is diminished in the early stages of the disease, even when no complications are present. Hewetson's observations seem to favor this view, the amount in his cases ranging from 228 to 400 gr. a day.

Uric acid is always increased early in the disease and may be three or four times the amount excreted in health. According to Zimmermann, the quantity increases up to the fourteenth day, and then diminishes. During convalescence, the amount falls below the normal. Deposits of lithates and urates may occur at any time during the course of the disease, but they have no significance.

The chlorides are greatly diminished in typhoid fever, and may even disappear altogether. This diminution may be partly due to the lack of chlorides in the food, and partly to the large amount of the salt carried away with the stools. Parkes, however, has reported a case in which the quantity was diminished, although the patient was on ordinary diet, and had neither diarrhœa nor pneumonia. Murchison concludes, therefore, that there is an absolute retention of chlorides in the system in typhoid fever. During convalescence they are again excreted as in health.

Albumin is not infrequently found in the urine in typhoid fever. It is present at some time in the course of the disease in from one-fourth to three-fourths of all cases. Out of 141 of my own cases, in which the urinary analysis was made, albumin was found in 69. H. P. Loomis found albumin present in 17 out of 54 cases in his wards in the New York Hospital. In 2 cases casts were present without albumin, and in 7 cases both albumin and casts were found. Osler reports a much higher percentage of albumin in his service in the Johns Hopkins Hospital. During the six years from 1889 to 1895, 389 cases of typhoid fever were treated in the hospital and albuminuria was noted in 303, or 78 per cent. The amount of albumin was usually small, in the majority only a distinct trace with the usual tests. Albumin generally appears in the course of the second week, though sometimes as early as the first week of the disease. The albuminuria is usually of short duration and the quantity of albumin small. Cases in which the albuminuria is persistent or the amount of albumin considerable are usually severe and of doubtful prognosis. Many such cases, however, end in recovery, and the albuminuria disappears entirely. Of the 19 cases in which albumin or casts were found by Loomis, 13 were severe and 6 mild. In 6 cases the albumin did not disappear after convalesence. In only 1 of the 6 cases was albuminuria present before the onset of the typhoid fever.

Casts are often present in the urine in typhoid fever. They are

usually of the hyaline and granular forms and few in number. They are generally associated with albumin, but are sometimes found even when there is no albumin, as in the two cases observed by Loomis. In 7 of my cases in which repeated tests were made, casts were present without albumin. They were present in one hundred and sixty-four of Osler's three hundred and eighty-nine cases, or in forty-two per cent. The casts do not necessarily add to the gravity of a case. They usually disappear with the passing of the albuminuria.

The severer forms of renal affection will be described among the complications.

Sugar is rarely found in the urine in typhoid fever. In fact, it has been known to disappear with the onset of the fever in patients with diabetes and to return during convalescence.

The *toxicity* of the urine is much increased in typhoid fever. This hypertoxicity is independent of the temperature and is not influenced by the amount of urine secreted. It is, however, considerably affected by different methods of treatment. The experiments of Roque and Weill show that in typhoid fever left to itself the toxins produced in the body are in part eliminated during the continuance of the disease, the urotoxic coefficient being double that of the normal. This elimination is, however, incomplete, the hypertoxic quality of the urine being evident for four or five weeks after the cessation of the fever. In typhoid fever treated by cold baths the elimination of toxic products is enormous during the illness. The urotoxic coefficient becomes five or six times greater than in the normal condition. This hypertoxicity diminishes as the general symptoms decline and the temperature falls, so that with the establishment of convalescence the elimination of the toxins is ended and the coefficient descends to normal. The cold bath is therefore an eliminative treatment; it has no specific action, inasmuch as it does not at all prevent the formation of the toxins, but it assures their expulsion as fast as they are produced. When typhoid fever is treated with antipyrin the elimination of the toxic products is very slight so long as the remedy is used, the toxic coefficient falling sometimes even below the normal. But during convalescence the discharge of the toxins takes place *en masse* for the space of five or six days. Antipyrin is therefore not a true antiseptic. It does not prevent the formation of the toxic substances, but does prevent their elimination in the urine. The effect of naphthol upon the toxicity of the urine in typhoid fever has been tested by Teissier, and his conclusions are that naphthol is a real antiseptic in this disease, inasmuch as it prevents the formation of toxic matters both during the course of the fever and during convalescence.

Typhoid bacilli are present in the urine in a large proportion of cases, but as a rule only when it contains albumin. They are found not only during the febrile period but also during convalescence. In many cases they are present in great numbers in the urine at the time of discharge of the patients from the hospital (Mark Richardson). On combining the results obtained by various investigators it appears that bacilli were found in about thirty per cent. of all urines examined; this percentage rises to forty in cases containing albumin in any amount (1 gm. or more to the litre). In one case they were found as early as the third day of the disease. Petruschky states that the bacilli may be absent during the fever and at the beginning of convalescence and then appear later. As a rule they disappear from the urine at the same time as the albumin.

The Diazo Reaction of the Urine.—In 1882 Ehrlich described a test which he believed to be of diagnostic value in doubtful cases. The test depends upon a peculiar color developed in the urine and foam by the action of diazo-benzene-sulphonic acid in the presence of an excess of ammonia. For performing the test the following solutions are employed: Solution A: Hydrochloric acid, 50 c.c.; distilled water, 1,000 c.c.; sulphanilic acid to saturation. This solution must be thoroughly saturated, allowed to stand some days before being used, and shaken up from time to time. Solution B: 0.5 per cent. solution of sodium nitrite in distilled water. This solution should be kept in a cool place and in a dark bottle and renewed every week. Solution C (test solution, to be freshly made for each day's testing): 40 c.c. of solution A and 1 c.c. of solution B. The hydrochloric acid acting upon the sodium nitrite liberates nitrous acid in a nascent state, which in time, by combining with the sulphanilic, produces the diazo-benzene-sulphonic acid. The test is performed as follows: Equal parts of solution C and of the suspected urine are thoroughly shaken together in a test tube and 2 c.c. of strong ammonia are then allowed to flow gently down upon the surface. If the reaction is present, a cherry-red or deep garnet band will appear at the junction of the ammonia with the mixture. Upon shaking the tube after the addition of the ammonia, a pink tinge is imparted to the foam and the entire fluid becomes of a uniform red color. After standing for some hours a characteristic olive-green precipitate forms in the test tube. If the reaction is not present, the color of the contact band may be yellow or orange or brown, but without any tinge of red whatever. The foam is usually yellow. The following rules are important: (1) The urine must be fresh and filtered; (2) the urine must be acid; (3) the test solution C is to be freshly prepared each day and accurately measured; (4) the sodium nitrite solution

must be accurately made and renewed at intervals of a week or ten days; (5) the color band should be held against a white background, the light falling upon it from behind the observer. It must not be held against the light.

Ehrlich believed that the diazo reaction was rarely met with except in typhoid fever. Clinical experience has borne out this view, and yet physicians are by no means agreed as to the exact value of the test. There is no doubt that the reaction is present in a large proportion of cases at some stage of the disease. In a large series of cases examined during a period of five years in Gerhardt's clinic, von Noorden found it absent in only one undoubted case. Edwards reports that it was absent in only 2 out of 130 cases examined by him in Osler's wards. On the other hand, Hewetson, in a later series of cases, found it present in only 136 out of 196 cases. It was more frequently present early in the disease than late, often disappearing soon after the patient's admission to the hospital. The average duration of the reaction was about thirteen days. The intensity seemed to bear no relation to the gravity of the case or to the height of the fever. Hewetson found the reaction distinct in many other diseases, notably tuberculosis in its various forms, measles, scarlet fever, pneumonia, and malarial fever. It was present in about thirty-four per cent. of the tuberculous patients treated in the medical wards, being most frequent in the cases of acute miliary tuberculosis.

I have myself made several series of tests of the diazo reaction and believe that it is to be found in about ninety-five per cent. of all cases of typhoid fever, provided they are seen in the first or second week of the disease. On the other hand, I have obtained the reaction (only exceptionally, however) in scarlet fever, measles, pneumonia, malarial fever, and acute tuberculosis as well as in many of the chronic diseases such as are found in hospital wards. A most distinct and typical cherry-red reaction was given by a case of myxœdema which was receiving twenty grains of thyroid extract a day.

The most recent and exhaustive study of the diazo reaction is that of Krokiewicz. He made no less than 16,167 separate tests in a total of 1,105 cases. His chief conclusions are as follows: (1) The reaction never appears in physiologically healthy urine; (2) it is always present in miliary tuberculosis, only diminishing in intensity just before death; (3) the occurrence of the reaction in pulmonary tuberculosis is indicative of an unfavorable prognosis; (4) in typhoid fever, even in mild, abortive forms, the diazo reaction appears always in the first or second week. Later it may be less marked or absent. It may be looked upon as a symptom of the disease, and so long as it is present the morbid process is not complete. The appearance of

the reaction in the urine during convalescence nearly always indicates a relapse. It thus appears that the diazo reaction is of great importance, not only from a diagnostic, but also from a prognostic standpoint, in both typhoid fever and pulmonary tuberculosis.

Complications and Sequelæ.

Respiratory System.

Laryngitis is an occasional complication of typhoid fever. It appears in various forms. There may be a simple catarrhal inflammation of the larynx, attended with cough and hoarseness or perhaps even loss of voice. Or the process may go on to ulceration, involving either the epiglottis or the walls of the larynx itself. If the epiglottis alone is affected, the consequences are not usually serious, though there may be some pain and difficulty in swallowing. The ulcers are superficial and heal readily. When the larynx is involved, the ulcers are situated on the posterior wall and may extend to the vocal cords. Extensive ulceration may be present without causing marked symptoms. Sometimes there is aphonia or dysphagia or tenderness on pressure over the larynx and the cough is laryngeal in character. Occasionally the inflammatory process extends to the perichondrium, causing perichondritis and even necrosis of the cartilages of the larynx. Ulceration of the larynx is extremely rare in this country. It is always a serious complication. Apart from its destructive action upon the structures of the larynx, it is always liable to excite acute œdema of the glottis, necessitating intubation or tracheotomy, or causing death by asphyxia. Œdema of the glottis, apart from laryngeal ulceration, is very rare, but it is occasionally met with. Murchison has known it to occur in conjunction with erysipelas of the head and face, and other observers have also reported cases of this kind. Pseudomembranous (diphtheritic) inflammation of the throat, occurring as a complication of typhoid fever, will be referred to in a later section.

Bronchitis is of such frequent occurrence in typhoid fever that, as already stated, it should be considered rather as a symptom (see page 633) than as a complication. When it affects the smaller bronchi it often causes bronchopneumonia or collapse of the lobules of the lungs. The bronchopneumonia may terminate in multiple abscesses or in gangrene.

Acute lobar pneumonia is a not infrequent complication of typhoid fever, occurring in perhaps ten per cent. of all cases. It may occur at any period of the disease, but is most common during the second

or third week. Occasionally, but very rarely, it marks the onset of the fever, and in such cases it may for a time mask the real nature of the disease. All the initial symptoms may be those of acute lobar pneumonia, and the symptoms of typhoid fever may not appear until a week or ten days have elapsed. Sometimes the pulmonary process and the typhoid process coexist from the beginning and run their course side by side. Again, cases have been observed in which there were no symptoms at any time except those of pneumonia, but on autopsy the intestinal lesions of typhoid fever were discovered. These three varieties of typhoid fever complicated with pneumonia have been grouped under the name of *pneumotyphus* by French and German writers. The nature of the pneumonic process in these cases is still under discussion. Some writers, perhaps the majority, believe that the pulmonary affection is due to the same cause as the intestinal lesion, that is, that they are both the result of the typhoid infection. Other observers maintain that the pneumonia is simply an accidental complication. Both the pneumococcus and the typhoid bacillus have been found in the affected lungs post mortem.

As has been said above, pneumonia occurs most frequently during the second or third week of the disease. When it develops at this time, the symptoms are usually not well marked, and it may easily be overlooked unless the chest is repeatedly examined. There is seldom an initial chill, the temperature may not be elevated, the pain in the side may be absent, the cough not increased, and the characteristic sputa are usually wanting. As a rule, the only symptoms are an accelerated respiration and a general impairment of the condition of the patient. On examination the physical signs of lobar pneumonia are found.

Hemorrhagic infarcts occasionally occur in the lungs, particularly in cases in which the action of the heart is feeble. The infarcts are the result of embolism of the pulmonary artery or of some of its branches. The emboli usually originate in a thrombus of the right ventricle of the heart. Sometimes, especially in cases in which the pulmonary embolism occurs during convalescence, the emboli are to be attributed to thrombosis of the veins of the lower extremities. With the exception of hæmoptysis, the clinical signs are usually not marked. The occurrence of hæmoptysis, in the absence of physical signs of tuberculosis or pneumonia, should always suggest the formation of an infarct, especially if there be cardiac weakness present. The anatomical consequences in the lungs of hemorrhagic infarcts depend upon the source and size of the emboli. Limited areas of bronchopneumonia may result, or a pleurisy with or without effusion, if the infarct be near the surface of the lung. Small infarcts

may be entirely absorbed and leave no trace. If the emboli are very large and lodge in the primary divisions of the pulmonary artery, death may be immediate. Should the embolus take origin, as is occasionally the case, from a bedsore or other purulent collection in the body, circumscribed pulmonary gangrene may be the result.

Pleurisy with effusion is an occasional complication of typhoid fever. Liebermeister noted it in 64 out of 1,743 cases in the hospital at Basle. Of the 64 cases, 21 resulted fatally. Liebermeister, however, does not believe that this great mortality represents the true influence of the complication on the death rate, as every case of pleurisy, however slight, was counted in the reports of the post-mortems, whereas among those who recovered there is no doubt that many cases of pleurisy, with little or no effusion, were overlooked. Pleurisy apparently seldom occurs alone; in all but seven of Liebermeister's fatal cases it was dependent on some affection of the lungs, such as pneumonia, gangrene, or hemorrhagic infarction. In some instances pleurisy was evidently the cause of death; thus in one woman, whose illness had run a mild course, the pleurisy which supervened terminated in empyema, which perforated the lung and caused pneumothorax. The termination of pleurisy in empyema appears to be not uncommon. Murchison described three cases of the kind, all of which ended in recovery, though one of the patients died a year later of phthisis.

Hypostatic congestion of the lungs takes place in a considerable proportion of cases of typhoid fever. It develops most frequently during the second and third weeks of the disease. It is always a serious complication. It is directly due to weakness of the heart, and is therefore most apt to occur in severe and adynamic cases. It is usually accompanied by more or less bronchial catarrh. As the prostration of the patient increases, passive congestion gradually takes place in the dependent portions of the lungs. The tendency to venous stasis is promoted by the long-continued recumbent position of the patient. The feeble respiration and imperfect expansion of the lungs also favor the effusion of serum into the pulmonary tissue. In some cases of hypostatic congestion, the air is completely driven out of the most dependent parts of the lungs and we have the condition known as splenization of the lung.

The symptoms of hypostatic congestion are accelerated and labored respiration, weak and quickened pulse, cyanosis of the face, and cold extremities. There may be little or no cough or expectoration, the patient being too feeble or too somnolent to make the effort to clear the bronchi. The earliest evidence of hypostatic congestion is to be obtained by physical examination of the chest, which should

be made as soon as the respiration becomes quickened. If the congestion is at all advanced there will be dulness on percussion over the base of both lungs behind, with feeble respiration, combined with coarse moist râles. According to Liebermeister, dulness over the lower posterior part of the lungs is probably due to hypostatic congestion, when it exists on both sides simultaneously, when it is accompanied by well-marked weakness of the heart, and when it has developed gradually and without any fresh exacerbation of fever. One hundred out of 1,420 patients in the hospital at Basle gave evidence of hypostatic congestion; 50 of the 100 died. In 45 of the 100 cases the records had been carefully kept, and it appeared that the hypostatic condition developed during the first week in 9 cases, during the second week in 10, during the third in 17, during the fourth in 4, and later than the fourth week in 5 cases.

Pulmonary œdema often accompanies hypostatic congestion, and is likewise dependent upon cardiac weakness. It also occurs independently of other pathological conditions of the lungs. In cases in which the circulation is extremely feeble acute œdema is liable to supervene at any time and with great suddenness.

Hæmoptysis occasionally occurs in typhoid fever although no tuberculous lesion can be detected in the lungs during life nor even post mortem. Osler reports two cases in which hæmoptysis occurred repeatedly and after death no disease whatever was found in the lungs. It is possible that the hæmoptysis in these cases was due to small hemorrhagic infarctions such as have been described above, and that they had been absorbed before death took place.

Pulmonary tuberculosis is a not uncommon late complication or sequel of typhoid fever. It is especially apt to occur in protracted cases attended with great emaciation. It is probable that in some cases, particularly in hospital service, the patient whose powers of resistance have been lowered by his long illness has acquired the infection from subjects of tuberculosis occupying beds in the same ward with himself. Now that the infectious and communicable nature of tuberculosis is better understood and successful efforts are being made to exclude tuberculous patients from the wards of general hospitals, it is to be hoped that pulmonary tuberculosis will be seen less frequently as a sequel of typhoid fever.

Acute general miliary tuberculosis is a rare sequel of typhoid fever. Hoffmann found it present four times in two hundred and fifty cases post mortem. Liebermeister states that he has seen one such case in private practice.

General emphysema of the subcutaneous areolar tissue has been observed in a few instances. It may occur as the result of a slough-

ing ulcer of the larynx through which air escapes into the tissues of the neck. Sometimes, according to Murchison, emphysema is caused by the ulceration of a small bronchial abscess or gangrenous cavity in the lung. Pneumothorax may also be induced in this way, according to the same writer.

Circulatory System.

Pericarditis is an extremely rare complication of typhoid fever. Occasionally, on post-mortem examination, evidences of recent pericarditis are found, although there may have been no clinical signs of the condition during life. Liebermeister holds that the cardiac lesion in these cases is simply an accidental complication and is no part of the typhoid infection. He, however, had the fortune to observe in one year four cases of pericarditis following typhoid fever, all of which terminated in recovery.

Endocarditis is also an infrequent complication in typhoid fever. There seems to be but little tendency to disease of the valves of the heart. A few instances of the malignant form of endocarditis have been reported by Liebermeister, Pepper, and others. The mitral and aortic valves are most frequently affected, but vegetations have also been found upon the tricuspid. In Liebermeister's case, the aortic valves were the seat of the endocardial inflammation, and there were, as a result, hemorrhagic infarctions in the kidneys and spleen, and double pneumonia, of which the patient died. In this case the endocarditis first developed during convalescence. It is rare that endocarditis, especially the simple form, can be diagnosticated with certainty during the course of the fever. Cardiac murmurs, when noted in typhoid fever, by no means indicate endocardial inflammation. They are generally due either to simple dilatation of the cavities of the heart or to degeneration of the myocardium, to be presently described.

Myocarditis is of frequent occurrence in typhoid fever, particularly in severe cases. Even in the milder cases it is probable that some cardiac degeneration is present. The lesion of the heart muscle does not differ from that found in other acute infectious diseases. It is probably an acute degeneration rather than an inflammation of the muscular tissue, though the term myocarditis is usually employed to describe the process.

The symptoms of myocardial degeneration do not appear, as a rule, until the disease is well advanced. During the first week the pulse is accelerated and often dicrotic, but the heart's action is usually strong and the valvular sounds are clear and distinct. In the second week in severe cases, or in the third week in those of milder

type, the signs of cardiac weakness first manifest themselves. In some cases a soft systolic murmur is heard, with its maximum intensity at the apex of the heart. The cardinal signs, however, of cardiac degeneration are, as was first pointed out by Stokes, the progressive diminution of the impulse of the heart and the impairment or complete absence of the first sound. The impulse may be entirely absent and is often replaced by a wavy, undulating movement in the præcordial region. At the same time the first sound gradually grows more feeble and may be completely lost. The second sound usually remains clear and distinct. Occasionally, it also loses its distinctness, or becomes reduplicated or, in rare instances, it may be wanting. Sometimes, as noted by Stokes and Murchison, the first sound becomes so shortened that the cardiac rhythm resembles that of the fœtus in utero. In some cases there is a marked intermission or irregularity of the heart's action. Hayem has described several cases in which the intermission took place at regular intervals, occurring in one case after three, in two other cases after four normal contractions. Occasionally, there is great dilatation of the cavities of the heart, especially of the right ventricle, as shown by the extension of the cardiac dulness towards the right. This condition has also been found post mortem in cases characterized by extensive degeneration of the cardiac muscle. The systolic murmurs referred to above are usually only temporary, disappearing with the increasing feebleness of the heart muscle or, on the other hand, as the heart recovers its strength.

Myocarditis is always a serious complication. Patients may and do recover, even when the symptoms of cardiac weakness have been very pronounced. There is always danger, however, of death by syncope or by collapse. There are also certain indirect evil effects of cardiac degeneration, some of which have been already described. Of these the pulmonary complications are the most frequent, namely, hypostatic congestion, pulmonary œdema, and thrombosis of the pulmonary artery. Ordinary venous thrombosis is not uncommon, especially in protracted cases. Thrombi also often form in the dilated cavities of the heart, and fragments of these may be detached and lodged as emboli in the various arteries of the body.

Venous thrombosis is a rather frequent complication of typhoid fever. It occurs, as a rule, during the period of convalescence; in rare instances it is observed as early as the third or fourth week of the disease. It usually affects the veins of the lower extremities, especially the femoral vein of the left side. In 24 cases observed in the hospital at Basle, the thrombosis occurred 18 times in the femoral vein, 5 times in the saphenous, and once in the popliteal. In the

large majority of cases the left leg alone is involved. Of 41 cases collected by Liebermeister and Murchison, the obstruction was confined to the left leg in 30 cases, to the right leg in 7, and in 4 cases both legs were affected. In a later series of cases collected by Keen, the left side was involved in 69, the right side in 23, and in 7 cases the obstruction was bilateral. The frequency of the thrombosis on the left side is explained by the fact that the right common iliac artery crosses (and compresses slightly) the left common iliac vein, thus favoring coagulation in the veins of the left leg.

Venous thrombosis in typhoid fever protracts the period of convalescence, but usually terminates ultimately in recovery. Of seventeen patients observed by Murchison, three died, but in each of the three cases death was caused by some other complication. There is, however, always danger that a portion of the thrombus may become detached and produce embolism of the pulmonary artery, as in a fatal case reported by Liebermeister. Fortunately, this accident is of extreme rarity. Moist gangrene with fatal issue is also a possible result of the venous obstruction. A few cases of the kind have been recorded. Generally, recovery from the fever is accompanied by complete restoration of the circulation in the affected vein. In exceptional instances, as in thrombosis in other diseases, the circulation may remain permanently impaired. I have observed one such case, that of a strong, vigorous man who had typhoid fever twenty years ago. The attack was severe and complicated with thrombosis of the left femoral vein, and convalescence was long delayed. Since recovery from the fever the general health of the man has been excellent and he has led a life of great physical activity. The tissues of the leg, however, are enormously thickened and from time to time he suffers considerable pain and discomfort.

Arterial thrombosis and embolism are occasional complications of typhoid fever. They occur most frequently during the second or third week, during the period of greatest cardiac weakness. Arterial thrombosis is the result of an obliterating endarteritis, involving all the coats of the vessel, with formation of a thrombus. The endarteritis is considered to be due to the specific typhoid infection. Embolism of the arteries, on the other hand, is simply the result of fragmentation and detachment of clots formed in a weakened and dilated heart. Hayem and Keen believe that the arterial obstruction is more often due to embolism than to thrombosis. If the obliteration of the vessel is complete and permanent it is followed by dry gangrene of the parts supplied by the artery.

Gangrene is a very serious complication of typhoid fever. Fortunately it is very rare, and many observers of large clinical and patho-

logical experience have never met with a case. Keen, however, has been able to collect one hundred and fifteen cases of spontaneous gangrene, complicating or following typhoid fever. The date of onset is most commonly during the third week of the fever or early in convalescence. The earliest time at which gangrene has occurred, according to Keen's investigations, is on the fourteenth day, and the latest is in the seventh week. The chief factors in the production of gangrene are the weakened action of the heart and the sluggish peripheral circulation. To these must be added the influence of the typhoid bacillus in promoting the coagulation of the blood, which is the cause of the obstruction in the vessels. The gangrene may be either dry or moist. If the obstruction is arterial, whether due to embolism or to thrombosis, the gangrene is of the dry variety. When the obstruction is in the veins, it results, as a rule, in moist gangrene. Occasionally, there is obstruction of both arteries and veins, and in such cases there may be a combination of both dry and moist gangrene. Age does not seem to have a very marked influence in determining the occurrence of gangrene. Of 140 cases, there were 26 cases under fifteen years, 64 cases between fifteen and twenty-five, and 50 cases over twenty-five years. As Keen observes, this does not differ much from the normal age distribution of typhoid fever. The influence of sex is more marked. Of 155 cases there were 90 males and 65 females, or about 3 males to 2 females.

Gangrene is especially apt to affect the lower extremities, also other peripheral regions of the circulatory system such as the nose and ears. The genitals also are frequently involved. Keen lays especial stress upon this distribution of gangrene. Of 214 cases in which the location is stated, in 126 it was in the legs, in 25 in the genitals and anus, in 16 in the nose and ears, leaving only 46 in which the face, neck, arms, and trunk were affected. These figures support Keen in his contention that the sluggish peripheral circulation rather than the bacterial infection is the chief agency in the production of gangrene. When the gangrene is of arterial origin, the two sides of the body are equally affected. When it is due to obstruction in the veins, the left side is much more frequently involved, for, as we have seen, venous thrombosis occurs upon that side in the large majority of cases. The symptoms need not be dwelt upon here. They are the same as in gangrene occurring in the course of other diseases.

Under the title of *gangrenous dermatitis* Stahl, of Philadelphia, has recently reported a remarkable series of cases of gangrene of the skin occurring among the soldiers who had contracted typhoid fever in the camps during the late war. The cases were all observed in the St. Agnes Hospital of Philadelphia. Of 144 soldiers 10, or 6.9

per cent., were affected. The trunk was most frequently the seat of the disease, and the dependent parts were not more often involved than were the anterior parts of the body. The face and neck, the gluteal region, then the genitals and the legs was the order of frequency of the occurrence of the disease. In only one case were the toes affected, and here the process extended and resulted in the loss of the foot.

The patients who had gangrene showed marked circulatory changes, varying from weakened heart sounds to well-marked arterial sclerosis and phlebitis. It usually developed during the later stages of the disease, when the fever had considerably abated. The rapidity of its development was a marked feature, the skin in some instances seeming to melt while the patient was being examined. Equally marked was the speedy healing of the necrotic areas and the entire absence of any scarring or deformity.

Stahl was unable to find any especial exciting cause for this unusual manifestation of the disease. The soldiers affected did not all come from the same camp. Nor was the affection confined to patients in one ward or one floor of the hospital, nor to those under the care of any set of nurses.

Hemorrhage may take place from various parts of the body in typhoid fever. Epistaxis and intestinal hemorrhage have already been described among the symptoms of the disease. Hemorrhage from the stomach is an occasional occurrence. Osler reports three cases, two of which ended in recovery.

Nervous System.

Acute meningitis is a rather rare complication of typhoid fever. The cerebral symptoms which are so commonly present are apparently dependent upon the toxæmia of the disease. At all events, evidence of inflammation of the meninges is very seldom found post mortem, even in cases which have been characterized by marked delirium and other symptoms of disturbance of the central nervous system. Influenced by the observations and opinions of Murchison and the older writers it has been generally believed that when meningitis does occur it is secondary to pyæmia or to disease of the middle ear or to a tuberculous process. Keen, however, is of the opinion that meningitis is not infrequent in typhoid fever and that it is often due to direct infection by the typhoid bacillus. He has collected a series of fifteen cases and in all the bacillus of Eberth was found—in twelve, it is expressly stated, "in pure culture." Keen believes that cases of cerebral meningitis are often overlooked by reason of the fact that the

head is frequently not opened in typhoid post-mortems unless the cerebral symptoms have been very prominent. The symptoms of acute inflammation are masked by the general stupor and are supposed to be only a part of the usual delirium of typhoid. Keen believes further that even in cases without marked cerebral symptoms examination of the brain will show meningitis and infection by the bacilli of typhoid to be far more frequent than has been supposed heretofore. In his fifteen cases both the dura and pia mater were attacked indifferently, and the exudate was sometimes serous, sometimes seropurulent, but in six it was distinctly purulent. As opposed to the views of Keen we may cite Liebermeister and Hoffmann, who state that in two hundred and fifty post-mortems (in all of which the brain apparently *was* examined) only four cases of acute meningitis were found. Gowers also observes that "acute meningitis is extremely rare in typhoid fever, according to pathological evidence, although its existence is often erroneously inferred from intensity of delirium." The question is an interesting one and deserves further investigation on the lines followed by Keen.

The diagnosis of meningitis in a disease so constantly accompanied by functional cerebral derangement is attended with many difficulties. Rilliet and Barthez lay stress upon the early occurrence of disorders of motility (strabismus, etc.), which are very precocious in meningitis, but never exist in the early days of uncomplicated typhoid. In true meningitis, also, an abrupt rise of temperature and absence of morning remissions are to be noted. In four of the cases collected by Keen, however, the diagnosis was first made at the post-mortem.

General convulsions are of extreme rarity in typhoid fever. Of 2,960 cases admitted into the London Fever Hospital from 1862–69, convulsions occurred in only 6. The convulsions are not necessarily due to nephritis. Of the 6 cases observed by Murchison, albumin was found in the urine in only 1; no cause for the convulsions was found in the other 5. Four of the patients recovered. Olser, in Vol. V. of the Johns Hopkins Hospital Reports, describes a case, the only one which has come under his observation.

The case was that of a man who on the ninth day of a very mild attack of typhoid suddenly developed a short, sharp, general clonic convulsion, beginning almost simultaneously in both arms. The convulsions were repeated throughout the day, and in about ten hours the patient died. The convulsions were general, but the more intense movements were on the right side. On autopsy, there was found thrombosis of the branches of the left middle cerebral artery. Dr. John Abercrombie has reported two cases of convulsions occurring in the course of typhoid fever, both patients being adults; in the first

case they were due to intestinal irritation, in the second to the passage of a portion of thrombus to the heart (?). Both patients recovered.

In children convulsions are also infrequent, but seem of graver significance. Of five cases recorded by Barthez, four were fatal. Sometimes the disease is ushered in with convulsions, but this is very rare. Holt has seen one case. Osler also refers to the case of a child of ten years who was admitted in coma, following a convulsion after a full meal. This was the starting-point of a severe attack of typhoid. Murchison quotes West as stating that convulsions followed by coma constitute a not uncommon mode of fatal termination in children.

Various forms of *paralysis* are met with during or after typhoid fever. They are sometimes due to a central lesion in the brain or spinal cord, but in the greater number of cases they are the result of a lesion affecting the peripheral nerves, a degenerative neuritis.

Hemiplegia of cerebral origin is a rare complication of typhoid fever. It is usually due to arterial thrombosis, less frequently to embolism. In very rare cases there is hemorrhage. Thrombosis of the cerebral veins may also be a cause of the hemiplegia. Of the reported cases, the majority occurred during the height of the fever. Osler describes 2 cases, in 1 of which the paralysis was preceded by convulsions. Of 17 cases collected by Hawkins and referred to by Osler, only 2 died, and in both of these a thrombus was present in the middle cerebral artery. In recent cases the prognosis is fairly good. In 14 of Hawkins' cases in which the result is given there were 9 complete recoveries.

Aphasia usually accompanies hemiplegia when the right side is affected. In twelve of Hawkins' cases the right side was paralyzed and aphasia was present in all. Aphasia, usually of a temporary character, is sometimes observed independently of any other paralysis. This is particularly the case in children. Morse has collected twenty cases of aphasia in children, in two of which it was due to embolism; in the others it was apparently not due to any organic lesion. In two-thirds of the cases it came on during convalescence, and in nearly all complete recovery took place in a few weeks. Gowers emphasizes the distinction between this post-typhoid loss of speech and real aphasia. There is no disorder of speech or partial loss, such as occurs in cases of organic disease of the brain; there is generally complete speechlessness. The patient can understand perfectly what is said and may be able to express himself by signs or even to write. In one case under Gowers' observation the condition developed gradually through disuse of the lips, which were dry and

cracked; the loss of the labial articulation rendered the words unintelligible, and they gradually ceased to be uttered. The condition may last for some weeks. In a case reported by de la Harpe, it was associated with general choreic movements.

Paraplegia or paraplegic weakness is not uncommon during convalescence. In some cases the symptoms are probably due to transverse myelitis. As a rule, the sphincters are not affected, the weakness being confined to the legs. There is seldom complete loss of power. The prognosis is favorable in most cases, although Gowers remarks that it is not uncommon for adults after typhoid fever never to regain the good walking powers they had before the illness, although there is nothing that can be called paralysis.

Acute ascending (Landry's) paralysis has been observed in a few cases. This affection often resembles very strongly certain varieties of multiple neuritis and is grouped with this latter disease by many writers. It is sometimes difficult to decide whether the case corresponds to the type of an acute infectious neuritis or to that of an acute myelitis. According to Strümpell, we must consider the possibility of an acute ascending paralysis in every paralysis of the lower extremities beginning acutely and accompanied by general symptoms, but only the further course of the disease can decide the question.

Acute anterior poliomyelitis occasionally occurs in typhoid fever, particularly in children. It is not always easy to distinguish it from neuritis. The abrupt onset, the absence of pain and other sensory symptoms, the rapid development of extreme paralysis, and persistent localized atrophy indicate a spinal lesion.

Peripheral neuritis, accompanied with limited atrophic paralysis, is an occasional complication or sequel of typhoid fever. It may develop during the height of the fever, but more commonly it does not occur until convalescence has begun. As in the neuritis following other infectious diseases it may be local or general in its distribution. It occurs apparently as often in mild cases as in those of severe type. It is sometimes very sudden and acute in its onset, or it may be gradual in its development.

Local neuritis in typhoid fever is limited, as a rule, to the extremities, one or more nerve trunks being affected. The arms and legs are attacked with equal frequency. The onset is usually attended with severe and sometimes agonizing pain in the arm or leg affected. There is usually tenderness along the course of the nerve trunks, and the muscles also are sore and sensitive to touch. The other symptoms of neuritis follow in well-developed cases. There is usually more or less paralysis, and sometimes considerable atrophy. The reaction of degeneration is present. The extensor muscles are chiefly

affected, and when the wasting is extensive and long-continued, there may be contractures due to overaction of the opposing muscles.

In rare instances the nerves of other portions of the body appear to have been affected as a result of the typhoid infection. Thus Gubler and George Ross each report a case in which paralysis of the palate was observed at the end of a mild attack of typhoid. In one of the two cases there was also paralysis of accommodation. C. Alexander also describes a case from the Breslau clinic in which, in addition to almost complete paraplegia, there was paresis of the left vocal cord, which, however, quickly passed away. In no one of these three cases was there any reason to suspect the presence of diphtheria. Paralysis of other cranial nerves has also been noted in a few instances.

Osler in this country and Handford in England have described an interesting condition following typhoid fever to which they have given the name of *tender toes*. The tips and pads of the toes become extremely sensitive so that the slightest touch causes pain. Sometimes the tenderness of the feet is so great that they have to be protected from the pressure of the bedclothes by a cradle. The pain occasionally extends to the pad of the sole of the foot, never to the dorsum. In one of Handford's cases the arms were also affected. There is never any redness or swelling, but in a few cases there is sweating confined to the feet and toes. Osler considers the condition to be due probably to a local neuritis, though there is no muscular wasting nor any definite loss of sensation. Osler had never seen a case of tender toes before the introduction of the Brand method of treatment into his wards in July, 1890. Since then he had observed twenty or more cases, all of which had been bathed. He was therefore inclined to regard the condition as an effect of the cold water. Handford's cases, however, had not been treated by the Brand method. The etiology of the affection is very obscure. Treatment had but little effect in relieving the pain, but all the patients recovered ultimately.

Multiple neuritis in typhoid fever may affect the legs alone, or both arms and legs may be involved. The condition is much more severe than local neuritis, though recovery appears to be the rule. Of four patients observed by Osler three recovered completely, and one made great improvement. The recovery, however, was very slow and gradual, in one case more or less paralysis persisting for a year. The fever in all four cases had been severe.

Muscular tremor, which has been referred to as a common symptom during the fever, may continue during convalescence. According to Gowers it has been known to persist and to be followed by the symptoms of disseminated sclerosis.

Tetany is sometimes met with in typhoid, usually during convalescence. In rare cases it has occurred during the first week of the disease. It appears to be much more frequent in some epidemics than in others. It is very rare in this country.

Chorea is an occasional sequel of typhoid fever. According to Holt it is not infrequent in children and is seen rather oftener than after the other infectious diseases. Gowers believes that the association of the two diseases is probably accidental, or at most the general disease only serves to excite the chorea in an indirect way. He instances, in illustration, the case of a girl, sixteen years old, who had a well-marked attack of chorea during the course of a typhoid; but it also appeared that she had suffered from acute articular rheumatism a year before.

Epilepsy is a rare sequel. The typhoid process probably simply determines the onset of epilepsy in a person already predisposed to the disease, as in the case of chorea. When an epileptic acquires typhoid the convulsions cease during the continuance of the fever, but return during convalescence. The same is true of choreic attacks.

Typhoid Spine.—Gibney has described a sequel of typhoid fever, to which he gave the name of "the typhoid spine" and which he regarded as a perispondylitis, "meaning an acute inflammation of the periosteum and the fibrous structures which hold the spinal column together." The disorder usually comes on late in convalescence, and sometimes not until the patient has been up and about for several weeks. Gibney described four cases in all of which the first symptom was severe pain in the back, usually in the lumbar region, and greatly increased on lateral or anteroposterior motion of the spine. There was no disease of the bone nor any pain in the distribution of the spinal nerves. In two of the cases there had been a fall after which the pain was greatly increased. Osler has met with several cases similar to those described by Gibney. In all of them there were well-marked nervous or hysterical symptoms, and Osler is inclined to regard the condition rather as a neurosis than a perispondylitis, although he thinks it not unlikely that under the designation of "typhoid spine" Gibney has described several distinct affections. All of the cases reported improved under massage and electricity and general tonics, and some of them apparently recovered completely.

Various *mental affections* may follow typhoid fever, especially when the disease has been severe and protracted. A condition of imbecility or stupidity sometimes develops and may last for months. *Melancholia* is perhaps the commonest form of mental derangement. *Mania* also occurs and may be very violent. These manifestations of nervous irritability are probably more frequent in those of heredi-

tary neurotic taint. Post-typhoid insanity is now generally regarded as due to nutritional disturbance, the result of nervous exhaustion and of insufficient food during the course of the fever. Wilson suggests the analogy to some forms of mania following starvation. Recovery is the rule, especially in cases of mania. According to Murchison, the other forms of mental derangement may last for months, but he had known of no instance in which they had been permanent. The memory, however, sometimes remains more or less impaired.

Organs of Special Sense.

Acute otitis media is a rather frequent complication of typhoid fever. It appears to be more common among hospital cases than in private practice. Hengst's statistics are the most recent and conclusive on this subject. He addressed a circular letter of inquiry to a large number of physicians, and received enough replies to give him an aggregate of 1,228 cases of fever. Out of this number there were 28 cases of acute *otitis media purulenta* reported, an average of 2.28 per cent. Six hundred and fifty-three were hospital cases, with 17 cases of otitis, an average of 2.6 per cent. Five hundred and seventy-five were cases from private practice, with 11 cases of otitis, an average of 1.9 per cent. It is probable that the percentage would be higher in private practice if all cases were carefully recorded. The complication usually develops from the end of the second to the fourth week, when the patient is in a condition of prostration and the mouth and nasopharynx are filled with catarrhal secretions, which the patient is too weak to expel. In Hengst's opinion, the usual mode of invasion of the middle ear is by extension of the catarrhal inflammation from the nasopharynx through the Eustachian tube, though it is possible that occasionally the process is caused by cold draughts of air on the side of the head, or by the entrance of cold water into the ear when the patient is being bathed. Purulent otitis media is probably always of microbic origin. Many varieties of bacteria have been found, either alone or in association. The pyogenic streptococcus and staphylococcus are the most common, but the diplococcus of pneumonia, the bacillus of Friedländer, and the bacillus of Eberth are also sometimes present. Mastoiditis developed in but 1 of Hengst's 28 cases, a case under his own observation, which was promptly relieved by an early and free Wilde's incision. All the cases terminated in recovery, no chronic aural discharge or impaired hearing resulting. Keen has collected 31 cases of otitis complicating typhoid fever, making a total of 59 when added to those of Hengst. Although this complication is most frequent in severe and protracted cases, yet not a single death is recorded among the 59.

The *ocular complications and sequelæ* of typhoid fever are rather numerous and some of them are of great importance. I shall not enumerate them all, but shall confine myself to those which occur most frequently, availing myself of the recent monographs by Bull and de Schweinitz.

Catarrhal conjunctivitis is very common, as it is in all fevers. According to Bull, the inflammation is usually confined to the palpebral conjunctiva, and there is seldom any secretion of mucus or sticking together of the lashes after sleep or swelling of the lids.

Phlyctenular conjunctivitis and *keratitis* are not uncommon during convalescence. The vesicles do not usually suppurate nor ulcerate, but discharge clear contents, and then dry up and leave no trace behind them.

Suppurative keratitis is fortunately a rare complication. It occurs in the third or fourth week of severe cases in which the nutrition of the patient has been greatly reduced or in cases in which the general treatment of the fever has been neglected. It usually terminates in sloughing of the cornea, with impairment or complete loss of vision.

Iritis and choroiditis are occasionally observed during the height of the disease, or during the period of convalescence. The inflammation is of serous or plastic type, and is never purulent, according to Bull.

Cataract, involving one or both eyes, sometimes develops during convalescence as a result of nutritional disturbances of the crystalline lens. The nutrition of the lens is especially apt to suffer in cases of choroiditis. De Schweinitz refers to a case, described by Trélat, in which double, semi-soft cataracts developed in a young girl during convalescence from typhoid fever. Romiée has analyzed 44 cases of cataract and attributes the pathogenic cause to typhoid fever in 17 (38.6 per cent.) of them.

Retinal hemorrhages appear to be not uncommon at the height of the disease. Bull has examined the eyes in about two hundred and fifty cases of typhoid and found hemorrhages into the retina quite frequently. De Schweinitz also is of the opinion that they are much more frequent than is generally supposed. They do not form the subject of complaint by the patient, unless they occur at the macula lutea, where they interfere markedly with vision. Often the patients are so lethargic or delirious that the presence of small hemorrhages does not attract their attention. According to Bull, small hemorrhages are often entirely absorbed, especially in young people. Profuse hemorrhages into the retina are rare. They sometimes manifest themselves in association with intestinal hemorrhage. Sometimes a profuse intestinal hemorrhage will cause amaurosis from the great

loss of blood, without there being any retinal hemorrhage. Should these patients recover, the blindness is usually permanent through atrophy of the optic nerve.

Optic neuritis may complicate typhoid fever even when meningitis is not present. It may be single or double. It may subside, leaving a moderate or slight impairment of vision, but is more apt to end in atrophy of the optic nerve.

Paralyses of the external ocular muscles are not infrequent during convalescence. They have been attributed to a chronic nephritis, but are more probably due to a neuritis caused by the specific typhoid poison. They usually terminate quickly in recovery. Dilatation of the pupil and paresis of accommodation have already been considered among the symptoms of typhoid fever.

Digestive System.

Pharyngitis is a frequent complication of typhoid fever. It is usually catarrhal and involves the tonsils and fauces in addition to the walls of the pharynx. As already observed, it may extend through the Eustachian tube and set up an inflammation of the middle ear. It frequently gives rise to a great deal of difficulty in swallowing, and may lead to superficial ulcerations. The pharynx may also be the seat of a membranous inflammation, which causes deep ulceration. This is a very serious but fortunately rare complication. Diphtheritic pharyngitis will be considered later among the diseases sometimes associated with typhoid.

Acute glossitis is an extremely rare sequel of the disease. Keen describes a case communicated to him by Osler. The patient was convalescent from a mild attack of typhoid, and had been free from fever for ten days before leaving the hospital. He returned three days later with his mouth open and the tongue enormously swollen and very tender. Osler thought at first that suppuration was about to take place, but in the course of three or four days the swelling subsided.

Noma or gangrene of the mouth is a rare complication of typhoid fever; Murchison met with it only once and states that it occurred in only one of six hundred cases observed by Griesinger. Murchison also affirms that it occurs only in children, but Draper has seen two cases in the New York Hospital, both of which were in adults. The disease is usually fatal.

Parotitis is a rather infrequent complication. The majority of cases result in suppuration with great destruction of tissue in the gland and its neighborhood. Among 1,600 typhoid-fever patients at Basle, there were 16 cases of suppurative parotitis, 7 of which proved

fatal. Parotitis without suppuration occurred 3 times. Murchison met with but 6 cases in all his experience—5 of the 6 patients died. Keen has collected a series of 75 cases following typhoid fever. The death rate in cases in which the result is stated is nearly 30 per cent. Twenty of the 28 cases in which the sex is named were males. In an earlier study of this affection Keen concluded that it was very rare in childhood, but as the result of his recent researches he has found 9 cases in children under fifteen years of age. Parotitis appears most frequently during the third or fourth week of the fever, but sometimes not until convalescence is established. On the other hand, Gilbert and Fournier have reported a case in which double suppurative parotitis began on the tenth day of the disease. It occurs, as a rule, only in severe cases and is always a dreaded complication. In the majority of cases only one side is involved, but occasionally both glands are affected. In favorable cases, the inflammation subsides and resolution takes place in a week or ten days. When pus is formed it may discharge either externally or into the external auditory canal, unless evacuated by incision and drainage. Death commonly occurs through cerebral thrombosis or septicæmia. In two cases tabulated by Keen there was facial paralysis from involvement of the seventh nerve. The cause of the parotitis is generally a secondary infection from the mouth through Steno's duct. In a certain number of cases there appears to be a metastasis of the typhoid poison. In two of Keen's cases, the bacillus of Eberth was found; in one case it was associated with the staphylococcus, but in the other the typhoid bacillus existed alone. Keen advises prompt surgical interference when suppuration occurs. According to Liebermeister, the frequency of suppurative parotitis has greatly diminished since the introduction of a systematic antipyretic treatment.

Ulceration of the œsophagus occasionally occurs. It is not usually attended with marked symptoms. Keen, however, reports two cases of stricture of the œsophagus which apparently followed upon typhoid ulcers resulting in cicatricial contraction. They are believed to be the only cases on record. The first case was that of a woman who entered Professor Osler's ward in the Johns Hopkins Hospital twenty months after recovery from a severe attack of typhoid fever. The fever had been complicated with profuse intestinal hemorrhage and also gastritis with accompanying vomiting. There had been no hemorrhage from the mouth, nor blood in the vomit. During the sixth week of her illness the patient had complained of some difficulty in swallowing. This steadily increased until at the end of the eighth week she was unable to swallow any solid food. Two days after her admission to the Johns Hopkins Hospital, Professor Osler attempted

to pass the stomach tube, but at a distance of 34 cm. from the teeth an obstruction was met which could not be overcome by any of the ordinary bougies. On the following day a filiform bougie 2 mm. in diameter was passed, and from that time on the stricture was gradually dilated until at the end of five weeks the patient was able to swallow some bread and meat.

The second case was that of a man who was admitted to the Philadelphia Hospital during the service of Dr. F. A. Packard. Twelve weeks previous to admission he had passed through a typical attack of typhoid fever during which he had hemorrhages not only from the bowels, but also from the stomach or œsophagus. In his case two strictures were found, one at a point 14 cm., the other 24 cm. from the teeth.

A filiform bougie was passed through the upper stricture, but the lower one was impassable. At the time the case was reported to Dr. Keen, the patient was still under treatment in the Philadelphia Hospital. The further history of the case has been recently published by Dr. F. S. Dennis, to whom the patient was brought for relief in March, 1898. At that time the œsophagus had become entirely occluded, and for months the patient had been unable to swallow anything and had been nourished by rectal enemata. He was greatly emaciated and cyanotic in appearance, and his temperature was subnormal. Dr. Dennis performed gastrostomy in such a way as to leave a fistulous opening without any peritoneum in contact with it, and consequently it had remained patent. The patient was presented by Dr. Dennis at a meeting of the New York County Medical Association in November, 1898. He had gained seventy-eight pounds in weight, although nothing had been taken by the mouth since the operation.

In neither of these two cases was there any history of traumatism or of venereal disease.

Hæmatemesis is a rare complication. It is not mentioned by the older writers, such as Murchison and Liebermeister. Osler describes three cases, in two of which blood was also passed from the bowel. The cause of the hæmatemesis is not given. Two of the patients recovered.

Ulceration of the stomach is probably not very infrequent in typhoid fever. It usually, however, produces no characteristic symptoms, and the ulcers are found only after death. In some cases they give rise to obstinate vomiting and even hemorrhage, or may lead to *perforation.* Keen says that hemorrhage from such ulceration without perforation is rare. Fenwick describes two cases, referred to by Keen, in which typical typhoid ulcers were found after death, appar-

ently originating in the solitary glands of the stomach. In one case there had been perforation, but the opening had been closed by adhesions to the liver. In this case there had been vomiting and severe hæmatemesis.

Perforation of the intestine is the most important and the most dangerous of all the complications of typhoid fever. The frequency of the accident is estimated variously by different writers. It occurred in 48 out of 1,580 cases under the care of Murchison, or in 3.04 per cent. Schulz, however, found that intestinal perforation took place in only 1.2 per cent. of 3,686 cases treated in the Hamburg hospitals during the years 1886 and 1887, his experience thus corresponding with that of Liebermeister, who states that perforation occurred in 1.3 per cent. of 2,000 cases in the hospital at Basle between 1865 and 1872. Murchison also found it much more frequent as a cause of death in fatal cases than have other observers. Of 325 autopsies made by him, perforation was present in 60 or 18.46 per cent., whereas of 1,309 autopsies reported by French and German observers (and tabulated by Murchison) it was noted in only 8.8 per cent. Recent writers make the percentage even less. Hölscher found perforation in only 6 per cent. of 2,000 cases, and Fitz, in 4,680 fatal cases collected from various sources, found it present in 6.58 per cent. Keen, in his careful study of intestinal perforation from a surgical standpoint, accepts Fitz's percentage as fairly representing its frequency.

The perforation takes place most frequently in the third or fourth week of the disease. It may, however, occur as early as the first week, or as late as the sixteenth week, as shown in the following table compiled by Fitz:

Date of Occurrence of Perforation.

Week.	Cases.	Per Cent.
First	4	
Second	32	16.5
Third	48	24.8
Fourth	42	21.7
Fifth	27	14.0
Sixth	21	13.4
Seventh	5	
Eighth	3	
Ninth	2	
Tenth	4	
Eleventh	3	
Twelfth	1	
Sixteenth	1	
	193	

Perforation is much more common in men than in women. All observers are agreed in this although unable to offer any explanation of the fact. Of 444 cases tabulated by Fitz, 71 per cent. were in men and only 29 per cent. in women. It is extremely rare in children. Fitz has collected from various sources 192 cases in which the age of the patients is given, and only 7 of the whole number were under the age of ten years. The rarity of the accident in children is probably to be explained by the mildness of the disease in the early years of life.

The seat of the perforation is usually the ileum, generally in the lower portion. Fitz and Hawkins have made independent investigations on this point, and on combining their figures it appears that of 239 cases, the ileum was perforated in 197 (82.4 per cent.). In 25 cases the opening was in the colon, in 8 cases in the vermiform appendix, in 7 cases in the cæcum, and in 2 cases in the jejunum. The portion of the colon most frequently perforated, according to Keen, is the sigmoid flexure, and he therefore concludes that if no perforation be found in the ileum, cæcum, or appendix, the next most likely point would be the sigmoid flexure. The perforation is almost uniformly single, but Fitz reports that out of 167 cases there were two or more perforations in 29.

Perforation of the intestine occurs most frequently in severe cases of typhoid fever. In a considerable proportion of cases, however, the previous symptoms have been mild. Fitz indeed holds that there is no definite relation between the severity of the individual attack and the occurrence of perforation, for in about one-fourth of nearly two hundred cases analyzed by him the course of the disease was distinctly stated as mild. Murchison also laid stress upon the fact that perforation may occur in cases of the mildest description, and Liebermeister states that it sometimes happens that the perforating ulcer is found to be almost the only one present in the entire alimentary tract. The occurrence of perforation is favored by the presence of indigestible food or hardened fæces or by overdistention of the bowel with gas. It may also be caused by vomiting, or straining at stool, or by sudden movements on the part of the patient. Murchison refers to a case of Morin's in which perforation resulted from the administration of an enema, and adds that many instances might be related in which it was produced by the injudicious administration of a purgative.

The symptoms of perforation are due to the resulting peritonitis and are usually well marked and characteristic. The occurrence of perforation is indicated, as a rule, by the *sudden* onset of severe pain in the abdomen, accompanied with symptoms of collapse. The abdomen becomes distended and rigid, with marked tenderness on pres-

sure. The pulse is small and rapid and there is frequently a temporary fall of temperature. Vomiting is common, the face grows pale and pinched, and the breathing thoracic. If the peritonitis becomes general the signs of prostration increase and the patient gradually sinks in collapse. In many cases, however, the symptoms are more obscure, and the existence of a perforation may not be suspected. Many or even all of the characteristic symptoms may be entirely wanting. In one-fourth of Murchison's cases there was no pain whatever, and the chief indications of the accident consisted in a sudden increase of prostration with a rise of the pulse and temperature and a distended, rigid state of the abdomen. Other writers have reported cases in which a rather sudden lowering of the temperature was the only symptom observed. Sometimes the symptoms develop gradually or in very sick patients may even pass entirely unnoticed. Of eighty cases collected by Fitz it was found that in fifty-six the onset of the symptoms was sudden, in fifteen cases the symptoms were gradual or latent, while in five there were no symptoms whatever of perforation. Keen quotes Armstrong as writing that in none of his cases "was the occurrence of perforation indicated by those well-marked, striking symptoms so generally mentioned in textbooks."

It is evident, therefore, that the diagnosis of perforation must sometimes remain in doubt. As observed by Liebermeister, the diagnosis is probable when we find the evidences of peritonitis present, especially when they have supervened suddenly. It must, however, be borne in mind that fatal peritonitis may arise during typhoid fever without perforation of the bowel. In rare instances the perforation is attended with the discharge of considerable intestinal gas into the peritoneal cavity. In such cases the normal hepatic dulness may suddenly disappear. This sign is of value, of course, only when previous examination has shown the presence of normal dulness over the region of the liver. Fitz attaches but little importance to this sign. The liver dulness may be obliterated by overlying loops of intestine or the liver itself may be abnormally small. As a matter of fact, he adds, the dulness is usually found to persist when the intestine is actually shown to be perforated. Keen believes that the presence or absence of leucocytosis may prove of value as an aid to the diagnosis of perforation. As stated on page 630, the number of leucocytes in the cubic millimetre at the beginning of the fever is about normal, but tends to diminish slightly throughout the course, reaching its lowest point towards the end of defervescence. The development of a local inflammatory process, except occasionally in very exhausted patients, is always accompanied by a certain degree of leucocytosis. In excep-

tional instances the white blood cells are increased with the fever, even without any complication. In 4 cases observed by Cabot the count was over 11,000 to the cubic millimetre, and ran as high as 17,-700 without any other than the typical typhoid lesions. The effect of inflammatory complications, however, even in such cases, is very marked. In one case reported by Cabot, the number of leucocytes five days before perforation was 8,300, but at the time of perforation it reached 24,000. In a second case the number was 18,500 at the time of perforation. Keen therefore advises that, if time allows, a blood count should be made in every case of doubt. The value of the test, however, would seem to be somewhat limited by the fact that the leucocytosis simply indicates the beginning of the peritoneal inflammation, which may or may not be due to perforation.

Perforation of the intestine is almost invariably fatal, and death sometimes follows within a few hours. Fourteen of Murchison's patients lived less than twelve hours after the symptoms began. Of 134 cases tabulated by Fitz, 37.3 per cent. were fatal on the first day, 29.5 per cent. on the second day, and 83.4 per cent. during the first week following the onset of the symptoms. During the second week 9 patients died, 4 during the third week, while 1 lived thirty days, and another thirty-eight days. In rare instances recovery has taken place. At least, cases have been reported by competent observers in which recovery has followed after all the symptoms of peritonitis from perforation. Liebermeister describes three cases in which the attack was very sudden and was followed at once by well-marked pneumatosis of the abdomen, and complete loss of liver dulness in front. Under the persistent use of opium complete recovery followed, and the normal percussion sound over the liver gradually returned. It is difficult to understand how recovery took place in these cases, for it is evident that in all a considerable amount of gas must have been discharged into the abdominal cavity. In cases related by other writers it is probable that there was but little or no escape of intestinal contents, or that the peritonitis was rapidly limited by adhesions. In some instances a circumscribed abscess results which may discharge by the bowel or open externally.

Peritonitis without perforation of the bowel may result from various causes. It may occur by direct extension of the inflammation from the mucous to the serous membrane. In this way, according to Murchison, peritonitis has been known to occur before ulceration has commenced, and even during the first week of the disease. It may be due to the rupture of a softened mesenteric gland or to softened infarctions in the spleen. Occasionally, it has been caused by an abscess in the ovary, or by abscesses in other parts adjacent to the

peritoneum. A number of cases are on record in which peritonitis has resulted from rupture of the gall-bladder, with escape of gall-stones or bile into the abdominal cavity. In one case the peritonitis was excited by suppurative inflammation of the mucous membrane of the gall-bladder, but the gall-bladder itself was intact. Severe general peritonitis, without perforation of the bowel, occurred in Basle 16 times among about 2,000 patients, with 13 deaths. This variety of peritonitis appears to be most frequent among women: of 16 cases 6 were in men and 10 in women. This is in striking contrast to the rule that applies in peritonitis due to perforation. It is usually impossible, according to Murchison, to distinguish during life between these different causes of peritonitis, but in the great majority of cases the cause is perforation of the bowel.

The *hepatic* complications and sequelæ of typhoid fever are not common, but are in some instances of great interest and importance. They are often masked by the general abdominal symptoms of the disease, and in many cases are only discovered after death. Often the symptoms are latent, or the condition of the patient is such that they pass unnoticed. During the past eight years the subject has attracted considerable attention and several important papers have been published, notably those by Dupré, Chiari, A. L. Mason, Osler, and Keen.

So-called *lymphomata* are of frequent occurrence in the liver in typhoid fever, but apparently have no clinical significance. A recent experimental study by Dr. Walter Reed has proved that these lymphomata are not composed of lymphoid cells, but that they represent foci of necrosis of the liver cells. Osler has proposed for them the name of "focal necroses." The foci are subsequently replaced by well-defined areas of localized connective tissue. It is probable that the necrotic areas are caused by the toxalbumins of the disease. These focal necroses cause no symptoms, so far as we know, but Osler suggests that it is quite possible that a widespread involvement of the liver lobules might cause an icterus gravis, which occasionally develops in typhoid fever, or lead to cirrhosis through their later connective-tissue change.

Abscess of the liver is an occasional sequel of typhoid fever. In a series of 21 cases collected by Keen, 16 were primary, the other 5 being secondary to typhoid lesions elsewhere. The primary abscess is solitary and in some instances is the direct result of infection by the typhoid bacillus; in others the pyogenic bacteria and the colon bacillus are the immediate cause. The secondary abscesses of the liver are multiple. In the few recorded cases they followed in 1 instance an abscess of the parotid, in 2 instances they were

secondary to abscesses of the hand, and in 2 others they were associated with perichondritis of the larynx. Of the 21 cases tabulated by Keen death occurred in all but 2. In 1 of the 2 cases the abscess ruptured through the diaphragm and discharged through the lung, and the patient recovered. One year later, however, the abscess recurred and again opened spontaneously, this time externally at a point near the right iliac spine. The opening was enlarged by an incision, and in due time the patient recovered completely. In the other case the pus discharged through the bowel, and at the end of four months the patient was entirely well. The symptoms of hepatic abscess in these two cases appeared between the seventeenth and twentieth day of the disease, after defervescence had taken place. In the second case there was jaundice which diminished with the free discharge of pus.

Suppurative pylephlebitis sometimes, but very rarely, follows typhoid fever. It is probably a result of thrombosis of the portal vein, in Keen's opinion. In a case reported by Lannois the typhoid bacillus, associated with other bacteria, was found in the pus.

Jaundice is a symptom of extreme rarity. Murchison met with but three cases in which it was present, all of which were fatal. Osler reports that there was not a single instance among the first five hundred cases treated in the wards of the Johns Hopkins Hospital. It appears to be more common in the tropics. Murchison was inclined to regard jaundice as an unfavorable symptom, but its significance probably depends upon its pathology which varies in different cases. Osler classifies the cases of jaundice in typhoid fever into four groups: (1) catarrhal; (2) toxic; (3) those associated with abscesses of the liver; and (4) those associated with gall-stones and cholangitis. Catarrhal jaundice is usually an early and transient symptom and has no influence upon the course of the disease. Osler describes a case in which the jaundice appeared first at the onset of a relapse, following severe gastric symptoms. The patient recovered. Toxic jaundice or icterus gravis is very rare. The pathology is probably not always the same. Several cases that have come to autopsy have shown the lesions of acute yellow atrophy of the liver. In some cases the jaundice is apparently the result of parenchymatous degeneration of the liver; in others it is possibly due to focal necrosis of the liver cells, as already suggested. Jaundice may be associated with hepatic abscesses when the suppurative process is very widespread. But few instances have been recorded. Romberg describes one case in which there was slight jaundice and the liver showed very extensive suppurating pylephlebitis. Jaundice may develop in typhoid fever in connection with gall-stones, but it is not a necessary symptom unless

there is obstruction of the common duct. It sometimes occurs in association with suppurative cholecystitis, even though gall-stones are absent. Cholangitis, whether catarrhal or suppurative, is probably invariably attended with jaundice.

Affections of the gall-bladder and bile-ducts are much more common than disease of the liver itself. Reference has already been made to the occasional occurrence of cholecystitis, sometimes resulting in ulcerative perforation of the gall-bladder, with consecutive peritonitis. The cholecystitis may be catarrhal or suppurative, and in about one-fourth of the recorded cases it was associated with gall-stones. According to Mason the subjects are mostly young, and several cases under ten years of age have been reported. The symptoms are "pain in the region of the gall-bladder and under the scapula; a palpable, very tender swelling that is dull on percussion, sometimes pear-shaped and visible, giving doubtful fluctuation, described in one instance as like that of a tense hydrocele." There is almost invariably a tender spot a little above and to the right of the umbilicus. If perforation occurs, these symptoms are merged into those of collapse and general or local peritonitis. The presence of gall-stones is believed to predispose to the development of cholecystitis. In rare instances the inflammation extends to the biliary passages and cholangitis results.

The importance of these affections has long been recognized, but it is only within the past few years that their significance has been understood. As observed by Keen, the discovery of the bacillus of typhoid fever has thrown an entirely new light on both the etiology and pathology of these complications. In 1890, Gilbert and Girode demonstrated the presence of the typhoid bacillus in the gall-bladder in a case of typhoid fever complicated with suppurative cholecystitis. In 1891, Dupré reported that he had not only found the bacillus present during the fever, but that he had obtained it in pure culture from the gall-bladder of a patient six months after recovery from typhoid fever. Other observers have continued these investigations, and it appears that the typhoid bacilli are present in the majority of cases. Chiari examined 22 cases and found the bacilli in 19. The more advanced the stage of the disease the more constantly were the bacilli found. Of 10 cases in the stage of ulceration or of healing the results in all were positive. The same was true of 3 cases which died in a relapse. Chiari lays stress upon the fact that in 13 of the 19 positive cases the walls of the gall-bladder were the seat of extensive pathological changes. In 3 cases the mucosa was apparently intact, but no sections were made of the walls. Jaundice was noted in only 1 of the 22 cases. The rarity of this symptom is attributed

by Chiari to the fact that in typhoid fever the secretion of bile is greatly diminished through the parenchymatous degeneration of the liver which is so often present in severe cases. Dupré * has suggested that the bacilli in the gall-bladder may be the direct agent in causing relapses in typhoid fever. An increase of food during convalescence, by causing an unusual flow of bile into the bowel, might cause a reinfection of the system through the intestine. Chiari approves of Dupré's suggestion, and in support of it refers to the fact that in his three cases of relapse the number of bacilli in the gall-bladder was very large.

Cholelithiasis is an important sequel of typhoid fever, and there are grounds for believing that the typhoid bacilli are an etiological factor in the formation of the gall-stones. Bernheim first called attention to this relationship in 1889. He stated that he had several times seen attacks of biliary colic during or after typhoid fever in persons who had never had such attacks before, and he suggests that the typhoid bacilli may possibly cause an alteration or stagnation of the bile and thus favor lithiasis. Dufourt in 1893, in a paper entitled, "The Rôle of Typhoid Fever in the Etiology of Biliary Lithiasis," described the cases of nineteen patients who had their first attacks of colic after severe typhoid fever. In twelve cases the first attacks came on within less than six months after the fever. Dupré and Chiari are also of the opinion that cholelithiasis is probably often caused by the entrance of typhoid bacilli into the bladder. Further support for this opinion has been recently furnished by the bacteriological researches of Milian, Hanot, and others, who have found the bacilli in the gall-stones themselves and in some cases apparently serving as a nucleus. Mason, Welch, and Keen, after a careful review of the evidence, all conclude that there is good ground for thinking that typhoid fever may determine the formation of biliary calculi in predisposed persons.

Abscess of the spleen is a rare complication or sequel. Keen was able to find only nine cases. One case arose in the course of the disease, four about the third week, and four as late sequels, three of them as late as the seventh and eighth week. Every case proved

* Dr. G. Fütterer has recently (Medicine, November, 1898) claimed priority in the discovery of the typhoid bacillus in the gall-bladder. His observations on two cases were published in the Münchener medicinische Wochenschrift, 1888, No. 19, two years before the paper of Gilbert and Girode referred to above. Dr. Fütterer concludes: "In view of these facts, I feel that I may justly claim to have been the first to discover the presence of typhoid bacilli in the gall-bladder. I also claim priority for expressing the opinion that the relapses of typhoid fever are caused by typhoid bacilli entering the intestines with the bile, a conclusion easily reached from these findings."

fatal. In one case the abscess ruptured, producing a fatal peritonitis. Three cases were discovered only at the autopsy.

Keen reports a case of *leukæmic spleen* which seems to have resulted from typhoid fever. Pain in the splenic region began during convalescence from the fever and shortly afterwards the abdomen began to enlarge. The symptoms continued, and when Keen saw he patient seventeen months later, the case presented all the features of advanced splenic leukæmia.

Genitourinary System.

Acute nephritis is a rather frequent complication of typhoid fever. Its frequency appears to vary greatly in different epidemics. Thus, Osler reports that in the first 229 cases of typhoid fever in the Johns Hopkins Hospital there were 21 cases (9 per cent.) of acute nephritis, whereas in a later series of 160 cases there were but 5 cases (3 per cent.) of nephritis and not one of them was of serious character. Nephritis may set in at the onset of the disease or during the height of the fever, or may first develop as a sequel during convalescence. When it occurs at the onset or early in the course of the fever, it may mask for a time the true nature of the disease and present all the symptoms of an acute exudative or hemorrhagic nephritis, such as headache, fever, nausea and vomiting, pain in the back, and œdema of the face. The urine is diminished or suppressed and contains much albumin, abundant casts, and usually more or less blood. Nephritis of this type—the *nephro-typhoid* of the Germans—is rare in typhoid fever. As a rule, there are few definite symptoms of the renal complication, often nothing but the evidence presented by the urine itself—albumin and casts in abundance. The prognosis is usually good, the patients generally recover, and the nephritis subsides. Seven of the twenty-one cases in Osler's first series died, five of perforation of the intestine. In no case was death due to the renal condition.

Pyuria is said by Osler to be not uncommon in typhoid fever. Ten cases in his wards have been studied by Blumer. In 2 cases the pus was present when the patient was admitted to the hospital; of the remaining 8 cases the pus appeared in 4 between the tenth and fifteenth day, in 3 between the twenty-second and twenty-eighth day, and in 1 on the forty-second day. In no case had the patients been catheterized previous to the appearance of the pus. Bacteria were associated with the pus in all cases, the colon bacillus in 7, the typhoid bacillus in 2, and the staphylococcus albus in 1. There were no clinical symptoms due to the pyuria and Blumer was unable to determine the origin of the pus. Of the 10 patients only 1 died, death

being caused by hemorrhage from the bowel. Blumer considers pyuria to be a complication of no gravity, and important only from its association at times with the typhoid bacillus, prophylaxis demanding that in these cases the patient should be retained in the hospital until the pus has disappeared.

Hæmaturia is of occasional occurrence in typhoid fever. It is more frequent in severe cases, but many patients recover in whom this symptom has been present. It is usually associated with acute nephritis, but, according to Hewetson, the amount of blood present in the urine appears to bear no relation to the grade of nephritis which exists. In most cases the blood comes from the kidney—in rare instances it has been found to be due to a cystitis. Sometimes hæmoglobin may alone be present, as in a case reported by Osler of acute hemorrhagic nephritis complicating typhoid fever.

Cystitis sometimes occurs during convalescence. It may follow prolonged retention of the urine or may be the result of the use of an unclean catheter. It is seldom attended with serious consequences.

Pyelitis is a rare sequel. It occurred in three of Osler's cases, in one of which it was associated with extensive membranous inflammation of the bladder.

Urethritis may arise spontaneously during convalescence. Keen describes the cases of two patients neither of whom had ever had any venereal affection. No catheter had been used in either case. The urethritis lasted from ten days to two weeks and subsided without treatment in both cases. A bacteriological examination was made in one case, and the discharge showed numerous cultures of various micrococci, especially the staphylococcus pyogenes aureus, but no typhoid bacilli or gonococci. I have seen one case, in a man who had been treated with subcutaneous injections of sterilized typhoid bacilli. Neither typhoid bacilli nor gonococci were found in the discharge.

Orchitis or *epididymitis* is occasionally observed. Keen has collected 32 cases. The disease is most common during convalescence. Of 29 cases, 1 arose during the second week, 7 in the third, and 21 after the third week. In 15 cases the inflammatory process was confined to the testicle alone, in 4 cases to the epididymis alone, and in 6 cases both testicle and epididymis were involved. Keen believes that the disease is due, as a rule, to a pure typhoid infection, and not to a mixed infection by the pyogenic bacteria. The typhoid bacillus has been repeatedly found in the tissues in both orchitis and epididymitis, and also in pure culture in the pus when suppuration has oc-

curred. Some cases are associated with urethritis. The infection usually terminates in resolution. Sometimes the testicle remains indurated. In six of the recorded cases suppuration occurred, five times in the testicle and once in the epididymis.

Abscess of the ovary is a rare sequel of typhoid fever. Keen has collected four cases, in three of which a bacteriological examination was made and typhoid bacilli in pure culture were found in the pus.

Gangrene of the genital organs has been observed in a few cases. It is more frequent in women than in men. Keen has collected a few cases in which there was more or less destruction of the scrotum, and gangrene of the penis has been noted by Fournier and others. In women the external labia are the parts chiefly affected, and the gangrene is occasionally followed by complete closure of the vagina and retention of the menstrual flow. In some cases gangrenous ulcers form in the vagina. They usually appear on the posterior wall and may lead to a rectovaginal fistula. Gangrene may involve the perineum or the anus in both sexes. In women it is generally by extension of the process from the vulva.

The *catamenia* sometimes occur prematurely with the onset of the fever, but without apparent effect upon the progress of the disease. Later in the course of the disease, and in convalescence from severe attacks, the menses are often absent for several periods.

Abortion or miscarriage is apt to be brought on in pregnant women. Fortunately, the disease is rare in pregnancy, but when it does occur it causes premature delivery in the majority of cases. Of 14 pregnant women under the care of Murchison, 2 carried the child through the attack and made a good recovery. Twelve miscarried, in 2 cases in the second week of the fever, in 1 case in the third week, in 6 cases in the fourth week, in 2 cases in the fifth week, and in 1 case in a relapse. The first effect of the loss of blood accompanying the abortion is a lowering of the temperature and an apparent amelioration of the symptoms. In some cases this effect is permanent. As a rule, however, the temperature rises again and the patient is worse rather than better than before. The mortality in pregnant women with typhoid fever is high. Of the 12 women who miscarried in Murchison's series 4 died.

Osseous System.

Arthritis is an occasional complication of typhoid fever. Keen distinguishes three forms, rheumatic typhoid arthritis, septic typhoid arthritis, and typhoid arthritis proper. The rheumatic and septic varieties are both very rare. They may affect only a single joint,

but are usually polyarticular. The rheumatic form may be followed by a multiple ankylosis. In most of the reported cases there was a previous rheumatic history. Septic arthritis, according to Keen, is the result of a mixed infection with the typhoid and the pyogenic bacteria. It runs the usual course of similar septic inflammations and frequently terminates fatally in spite of all treatment.

Typhoid arthritis proper is sometimes polyarticular, but far more frequently involves only one joint. The multiple form may affect any of the joints, but is rather more common in those of the lower extremity. None of the recorded cases ended fatally. Ankylosis is a very frequent result, but can probably always be prevented by the early use of passive motion. Monarticular typhoid arthritis affects the larger joints, such as the elbow and shoulder, the ankle and knee, but particularly the hip. This form of arthritis is of great importance because of its tendency to result in spontaneous dislocation. Of eighty-four cases collected by Keen, forty-three were followed by dislocation, forty times in the hip, twice in the shoulder, and once in the knee. The arthritis usually arises during convalescence and leads to a gradual serous distention of the joint with relaxation of the ligaments. The symptoms are not usually marked, though there is often some pain, and in some cases swelling has been noted. In nearly one-half of the cases the actual dislocation was the first fact observed. Reduction is generally easy when the luxation is discovered early, but always difficult and often impossible when the discovery or proper treatment is delayed. The great majority of the patients were young people, thirty-two out of thirty-five being under twenty years of age. Keen therefore advises careful watching and repeated examination of the hip-joint in young persons to detect pain or any effusion.

Necrosis and other forms of bone lesion are very important sequelæ of typhoid fever. In rare instances, the disease of the bones arises during the course of the fever. Of one hundred and eighty-six cases collected by Keen, the date of onset was as follows:

In the first two weeks	16
From the third to the sixth week	66
From months to years after the fever	104

From this table it appears that the process begins almost always during convalescence and in over one-half the cases after convalescence is well established. Of the various forms of bone disease, necrosis and periostitis are the most frequent. The following is Keen's series of 1896:

Necrosis	35 cases.
Caries	1 case.
Periostitis	107 cases.
Osteitis (bone abscess)	12 "
Osteomyelitis	10 "
Granuloma	2 "
Exostosis	1 case.
	168 cases.

The tibia is the bone most frequently attacked. Next in order of frequency come the ribs and costal cartilages, the femur, the ulna, the humerus, the vertebræ, and the superior maxilla. In contrast with typhoid arthritis, typhoid affections of the bones are more frequent in adults than in children, two-thirds of the cases being in patients over the age of twenty years.

The disease is due to local bacterial infection; in the majority of cases the bacillus of Eberth is present. Of fifty-one cases in which a bacteriological examination was made, the pyogenic bacteria were found in thirteen, and in the remaining thirty-eight the typhoid bacillus was found, often in pure culture. In some cases there is also the history of injury or of muscular strain in the regions involved. The disease is usually chronic in its course, with but little tendency to spontaneous recovery, except after long periods of time. The general health, however, is but little disturbed, the affection seeming to be almost purely local. Treatment to be effective must be thorough. Complete excision of all the diseased tissue is followed, as a rule, by a prompt and permanent cure.

Skin, Connective Tissue, and Muscles.

Furuncles are observed quite often in convalescence, especially in severe and protracted cases. It is thought by some writers that they are more frequent in cases treated by the Brand method.

Abscesses of the skin and cellular tissue are not infrequent. They are most apt to develop at points which are subjected to constant pressure. In some cases, on the other hand, they may appear in any part of the body indifferently and seem to be a manifestation of typhoid or post-typhoid pyæmia. Chart No. 7 is from a case in which abscesses continued to appear during a period of thirty-six days. The case was severe from the outset. The patient was delirious and passed fæces in bed during the second and third weeks of the disease. On the seventeenth and eighteenth days he had several hemorrhages from the bowels. A large bedsore developed over the sacrum and smaller ones on the hips on about the twentieth day of the disease.

These were followed on the twenty-third day by numerous abscesses on the back, buttocks, and near the rectum, on the legs and arms, and in both axillæ. One very large abscess involved the cellular tissue beneath the right deltoid muscle. The patient ultimately recovered and was discharged on the sixty-sixth day of the disease.

Bedsores were formerly among the most common and dreaded sequelæ of typhoid fever. At the present day, they are seen with much less frequency. They have been defined as "gangrene under pressure" and are found most frequently over the sacrum. They may develop at any point that is subjected to pressure, such as the nates, the heels, the shoulder blades, the elbows, the occiput, the trochanters, and the crest of the ilium. They are naturally most frequent in emaciated persons and after protracted fever. They usually appear during the third or fourth week. Sometimes bedsores will originate in furuncles or in an abscess accidentally situated at a point exposed to pressure, as over the sacrum. As a rule, however, they may be prevented by careful attention to the skin of the patient and by changing his position frequently. Gangrene of the skin occasionally occurs at points that are free from pressure. (See Gangrenous Dermatitis, page 660.)

Rupture of the muscles sometimes takes place as a result of degeneration of the muscular tissue. It is most frequent in the muscles of the abdomen and is often accompanied by hemorrhage into or between the muscles. There are usually no clinical symptoms, but occasionally it results in suppuration and death from septicæmia.

Falling of the hair is a common sequel of typhoid fever, especially after severe cases. The changes in the nails have already been referred to.

Relapses.

A relapse in typhoid fever is a recurrence, after convalescence is apparently established, of all or most of the symptoms of the original attack. A simple recrudescence of fever often occurs during the stage of defervescence and should not be confounded with a true relapse. Recrudescences are usually transitory, lasting but a day or two and are often apparently due to indiscretion in diet or to constipation or to unusual excitement or fatigue. Osler, following von Ziemssen, insists that two of the three important symptoms—step-like temperature, roseola, and enlarged spleen—should be present to determine the diagnosis of a relapse. In some cases, however, the rash is absent and it may be impossible to demonstrate the enlargement of the spleen, and yet the presence of continued fever, attended with headache, loss of appetite, and more or less marked gastro-intestinal symp-

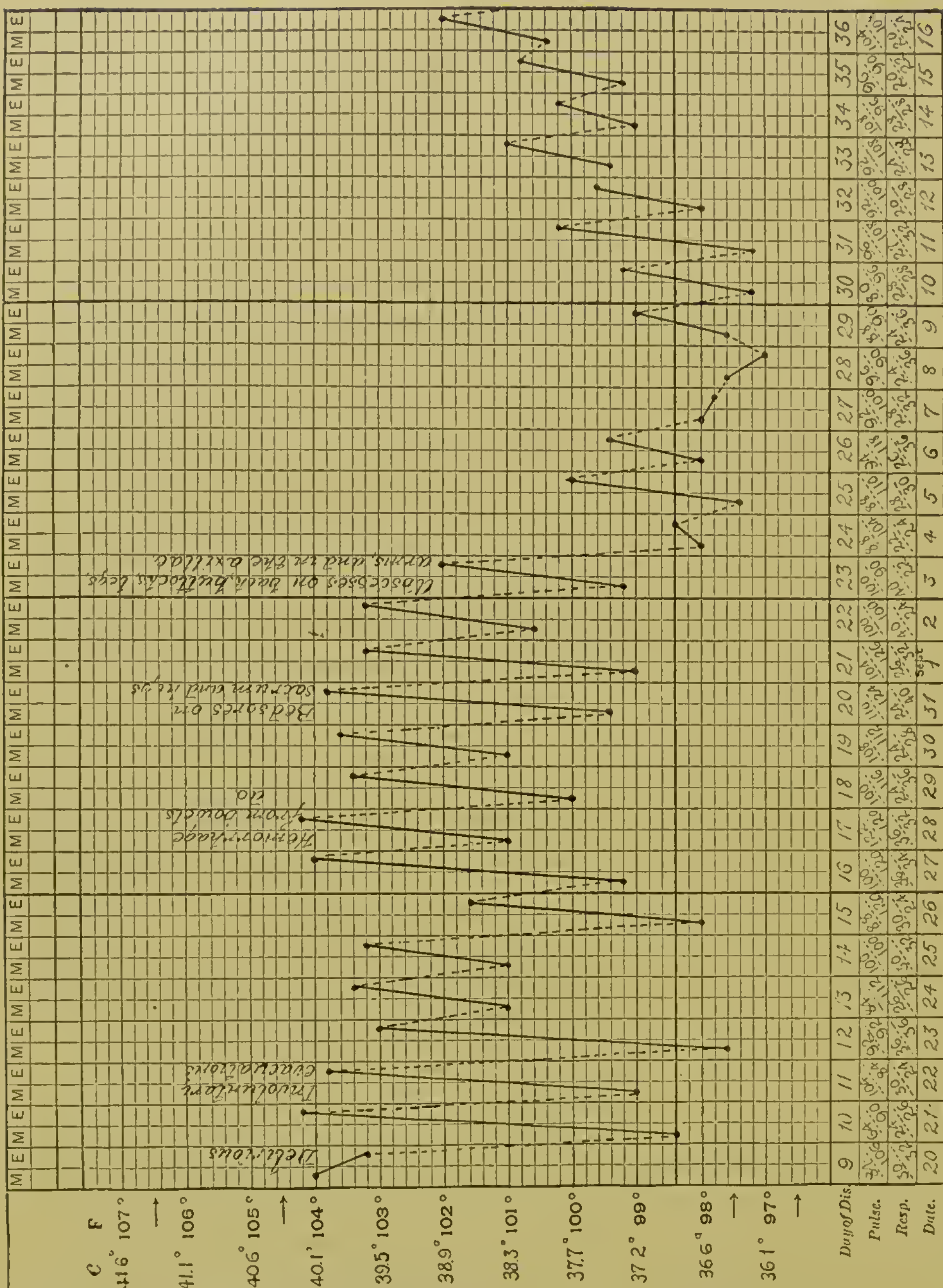

CHART No. 7.—Typhoid Fever Complicated with Multiple Abscesses. Post-typhoid pyæmia. The dotted lines indicate night temperatures.

toms, indicates that the patient is suffering a relapse. In such cases, as indeed in all cases of supposed relapse, inflammatory complications must be carefully excluded before the diagnosis can be made with certainty.

Relapses appear to vary in frequency in different epidemics. The lowest percentage is reported by Murchison, who noted relapses in only 80 out of 2,591 cases, or in 3 per cent. In 178 cases of which I have complete records relapses occurred in 14, or in 7.8 per cent.

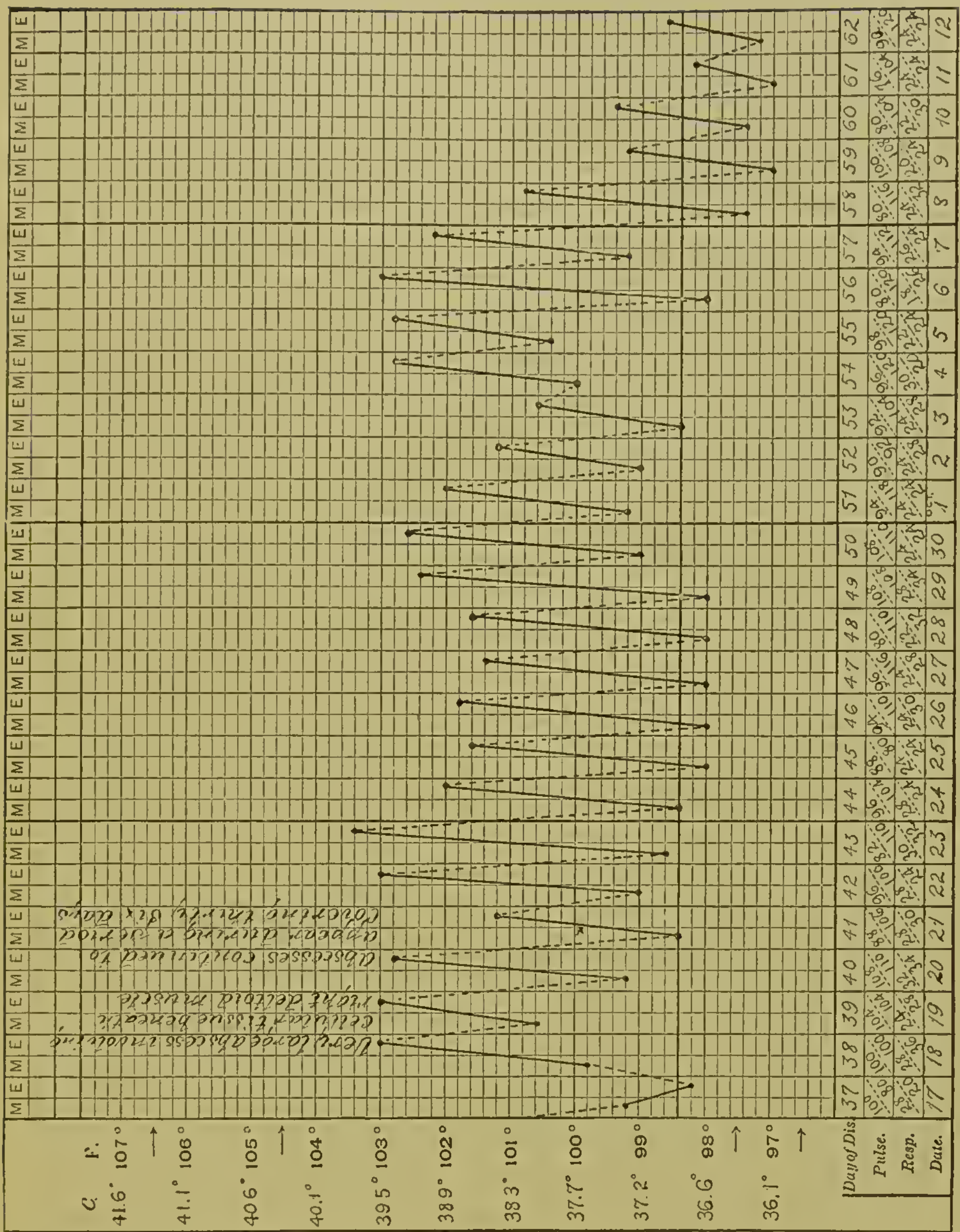

CHART No. 7.—Continued.

On the other hand, F. C. Shattuck, Henoch, and Immermann have observed relapses in over 16 per cent. of the cases under their care. Of 11,640 cases collected from various sources, relapses occurred in only 706, or in a fraction over 6 per cent. The larger the number of cases in a series, the smaller, as a rule, is the proportion of relapses.

The apyretic interval between the original attack and the relapse may be as short as two days or may extend to thirty-one days (Michel). In the large majority of cases, the duration of the interval is from eight to fourteen days. By a coincidence that is curious and perhaps not without significance, this is also the duration of the

period of incubation of the disease. In 51 cases, analyzed by Murchison, the period of apyrexia was seven days or less in 5; from eight to fourteen days in 38, and fifteen days or over in 8, the average duration being eleven days. In my own experience relapses have occurred so often in the fifth week of the disease, that is to say, about one week after the end of the original attack, that I am accustomed to refer to the fifth week as the week of relapse. Sometimes there is no definite period of complete apyrexia. The temperature approximates normal for two or three days and then rises again with a recurrence of the symptoms of the original attack. In eleven of Shattuck's cases, referred to by Osler, the relapse began before complete defervescence had taken place. Were such intercurrent cases excluded, the frequency of relapses would appear to be much less than it really is. Osler also reports four such cases and believes that they should be considered cases of genuine relapse. There were four cases of intercurrent relapse in my series. Were they included, the percentage would be increased to ten. Murchison also admitted that it was possible that a true relapse might occasionally overlap the primary attack without any apyretic interval, and that this might be the explanation of certain cases of enteric fever which are unusually protracted, but he adds that post-mortem examinations of such cases are still wanting.

The duration of the relapse is usually shorter than that of the original attack. In Murchison's cases, the average length of the first attack was twenty-six days, that of the relapse fifteen days. In only 5 of the 51 cases was the relapse longer than the original attack of the disease. Liebermeister, however, reports that of 111 cases at Basle, the fever lasted longer with the relapse than with the original attack in 37 cases, or exactly one-third. In 6 cases the duration of the two attacks was the same. The relapse is also usually milder than the primary attack, although, as noted by Liebermeister, the same complications are liable to occur as with the original fever. The onset is generally more abrupt, the temperature rises more rapidly, often reaching its maximum on the second day. The eruption appears earlier, as a rule, but is usually not so abundant as in the first attack (Jaccoud). Of 38 cases analyzed by Murchison, the rash appeared on the third day in 7; on the fourth in 8; on the fifth in 7; on the sixth in 2; on the seventh in 12; and at a later date in 2. The enlargement of the spleen takes place earlier. In fact, according to Gerhardt, the spleen remains enlarged throughout the interval of apyrexia. Sometimes the relapse is severe and protracted, although the original attack may have been mild. In one-third of Murchison's cases the symptoms were more severe in the relapse than

in the primary attack. The relapse usually terminates in recovery, but this is not always the case. Of Murchison's 51 cases, 7 were fatal, 2 from perforation, 2 from peritonitis due to infarction of the spleen, and 1 from abortion. A number of authors have reported cases in which a second or even a third relapse has occurred. According to Osler, Da Costa has twice seen five relapses.

Relapses are dependent upon a reinfection with the typhoid poison, and it is now generally believed that the second infection is from within the body, not from without. The clinical phenomena are accompanied by a renewal of the lesions of the intestine, and on post-mortem examination in fatal cases the recent lesions of the relapse are usually found lower down in the bowel than the cicatrizing ulcers of the original attack. We know but little of the etiology of the relapse in typhoid fever. Hamernjk, and later Maclagan, have maintained that relapses are due to inoculation of the healthy Peyer's patches by the sloughs thrown off by those first affected. This view seemed to derive support from the anatomical situation of the lesions of the relapse. On the other hand, as noted by Murchison, the fresh lesions in some cases are higher up in the ileum than those of the first attack. Maclagan also believed that relapses are more frequent in cases characterized by constipation during convalescence. General experience is, however, opposed to this view, relapses occurring quite as often in cases in which diarrhœa had been present as in those in which the bowels had been confined. Perhaps the most satisfactory theory of the etiology of relapses is that of Liebermeister. He believed that part of the typhoid poison remained latent somewhere in the body, not developed during the first attack and not destroyed nor expelled, and only in need of some exciting cause to bring it into activity. Liebermeister wrote at a time when the bacterial nature of the typhoid infection had not been demonstrated, but his view has received singular confirmation in the observations of Dupré and Chiari. As already stated, these observers found the typhoid bacilli almost constantly present in the gall-bladder of patients suffering from typhoid fever, and suggested that these bacilli might be the direct agents in causing relapses. So long as the bacilli remain in the bladder, they apparently do no harm, except perhaps locally. It is probable, also, that they may be discharged into the bowel without reinfecting the patient, provided this does not occur until after he has become immune against a second attack of the disease. If, however, this occurs before immunity has been acquired, then the patient is liable to suffer a relapse. This view enables us to account for the relapses which so often follow promptly upon indiscretions in diet before convalescence has become thoroughly established. The

more liberal diet stimulates the liver and causes an increased flow of the bacteria-laden bile into the intestine at a time when the patient is not protected against reinfection.

Association with Other Specific Diseases.

Typhoid fever is sometimes complicated by other specific diseases. The presence of one infectious disease does not protect the patient from another infectious disease, but rather renders him more susceptible to it by lessening his powers of resistance. Given the proper exposure, there is no reason why the sufferer from typhoid fever should not contract any of the other specific infections. In some cases the two diseases coexist, in others the second infection does not manifest itself until the patient is convalescent from the first.

Scarlet fever and typhoid fever are occasionally associated in the same individual. Murchison states that in former times when it was the practice in the London Fever Hospital to treat all forms of fever in the same wards, it was not uncommon for a patient suffering from enteric fever to contract scarlet fever. In eight cases under his observation the eruptions of the two diseases coexisted. In some cases the two infections acted upon the system simultaneously, in other cases in succession. In several cases there was reason to think that the typhoid as well as the scarlet fever poison had been contracted before the patient's admission to the hospital. Murchison was of the opinion that scarlet fever predisposed to typhoid fever. The majority of his cases made a good recovery, though convalescence was sometimes protracted.

Measles may develop during the course of typhoid fever or during convalescence. The association of the two diseases is naturally most frequent in children. Wilson refers to the following interesting case orginally reported by Chrystie:

> A boy twelve years of age was doing fairly well during the third week of a well-marked attack of typhoid when, on the sixteenth day of his attack, two other children in the house developed measles; on the twenty-third day the enteric-fever patient showed symptoms of measles; five days later his respiration became embarrassed, and he died in convulsions with a temperature of 105°.

This case illustrates the unfavorable effect which measles so often exerts when it complicates the specific fevers of childhood.

Smallpox and *chickenpox* occasionally complicate typhoid fever, more commonly during convalescence than during the height of the disease. Murchison has reported a remarkable case in which smallpox, vaccina, and typhoid fever all coexisted in the same individual.

Whooping-cough has been observed, though rarely, during the course of typhoid fever. Gillespie has reported a case.

Diphtheria is said by Wilson to be not infrequently associated with typhoid fever, particularly in children. I have seen one such case in an adult.

The patient, a man 23 years of age, was admitted into the Willard Parker Hospital, November 5th, 1897, with the following history: Ten days ago he had a chill followed by sore throat lasting a day or so. Since the beginning of the illness he has suffered chiefly from weakness, loss of appetite, and headache. He has been in bed most of the time, bowels said to have been regular, and has perspired freely. On admission, the throat was injected, with a few patches of mucus on tonsils and fauces. The Klebs-Loeffler bacillus was found in pure culture. The patient was considerably prostrated, and it was evident that he was suffering from some other disease in addition to diphtheria, the appearance of the throat not being sufficient to account for his condition. The axillary temperature was 101.6°, the face was flushed, the tongue dry and tremulous. There was also tremor of the hands. The abdomen was moderately tympanitic and there was tenderness in the right iliac fossa. There were a few fairly well-marked rose spots on the abdomen. The spleen could not be felt, but the area of dulness was somewhat increased. On the following morning the rectal temperature was 104.8°. The eruption on the abdomen had extended and the diagnosis of typhoid fever was made. The disease ran a rather severe course, but the patient made a good recovery, the temperature reaching normal on the fifteenth day after entrance into the hospital. There were no complications or sequelæ.

In some cases of typhoid fever complicated with diphtheria, as in a case reported by Murchison, it would appear that the specific nature of the throat affection was not recognized until the appearance of postdiphtheritic paralysis. Such cases emphasize the advisability of making a culture from the membrane in all cases of pseudomembranous inflammation of the pharynx and larynx, in order to determine the presence or absence of the Loeffler bacillus.

Typhus fever has often been observed in association with typhoid fever. Moore, of Dublin, believes, indeed, that in former days, when the essential difference between typhus and typhoid had not yet come to be recognized, it may even have been the rule for these two fevers to run their course concurrently—the enteric-fever cases contracting typhus in the wards in which they were placed for treatment.

Malarial fever and typhoid fever may coexist in the same patient. This association is, however, rare. Osler reports that of six hundred and eighty-five cases of typhoid fever in his wards, the majority coming from malarial regions, in not a single instance were the malarial parasites found in the blood during the fever. In three cases there was a definite history of malaria within a few weeks of the onset of the ty-

phoid fever, but in no case were the manifestations of the two diseases concurrent. A number of authentic cases has, however, been reported, in which the plasmodia of malaria have been found in the blood during the course of typhoid fever. Gilman Thompson was one of the first to call attention to the occasional concurrence of the two diseases.

During the past winter there were in Bellevue Hospital several instances of such association among the soldiers who had recently returned from Santiago de Cuba. The following case is that of a patient who was under my observation throughout his illness:

Patrick Darby, aged 22 years, private in Eighth United States infantry, was admitted to Bellevue Hospital September 1st, 1898. His health had been perfect until his present illness, and he was well and on duty every day while in Cuba. About August 16th, while en route to the United States, he had a chill followed by fever and sweating. The fever continued on the transport and afterwards at Camp Wikoff. He had mild chills occasionally. He had headache and felt dizzy a good deal of the time. No epistaxis. Slight pains across the loins. Restless at night. Appetite fair. Bowels regular, no diarrhœa. He got out of bed to come to Bellevue to visit his brother. He then had high fever, felt dizzy, and asked to be admitted to hospital. He has been growing weaker for the past ten days.

On admission, patient's temperature was 103°, pulse 84, respiration 24. His face was flushed, eyes somewhat suffused, and he seemed very weak, although well nourished. The tongue was slightly coated and tremulous. The lungs and heart were normal. The splenic dulness extended from the eighth rib to the costal border, but the spleen itself could not be felt. There was no rash. The urine was free from albumin and the diazo reaction was negative. The Widal test also gave negative results, but intracorpuscular hyaline bodies were found in the blood. The case was therefore regarded as one of malaria, although it was noted that the patient's anæmia was not so marked as in the other malarial cases among the soldiers in the ward, the percentage of hæmoglobin being 88, and the number of red cells 3,080,000 to the cubic millimetre. The patient was put upon full doses of quinine on September 2d, and during three days the temperature gradually fell, reaching 99° F. on the morning of the 4th. On the following day, however, the temperature rose again, and the treatment was changed to Warburg's tincture, one-half ounce being given three times a day, but without apparent effect. The patient became more and more prostrated and the fever continued to increase, as shown in Chart No. 8, reaching 104.2° on September 10th.

On the same day the edge of the spleen could be felt, and on the 12th the following note was made in the records: "Since September 8th the patient's temperature has followed a different type, being higher each day than on the preceding day. The tongue is coated white with clean edges. Patient looks sicker and is much more drowsy. Edge of spleen still felt below costal border." The Widal test now (the 12th) gave a positive result and the cold-bath treatment was begun. Only five baths were needed, the effect of each bath

being very marked, reducing the temperature from two to three degrees and lowering the pulse from four to thirty beats in the minute. There was no rose-rash at any time, but on September 22d the Widal reaction

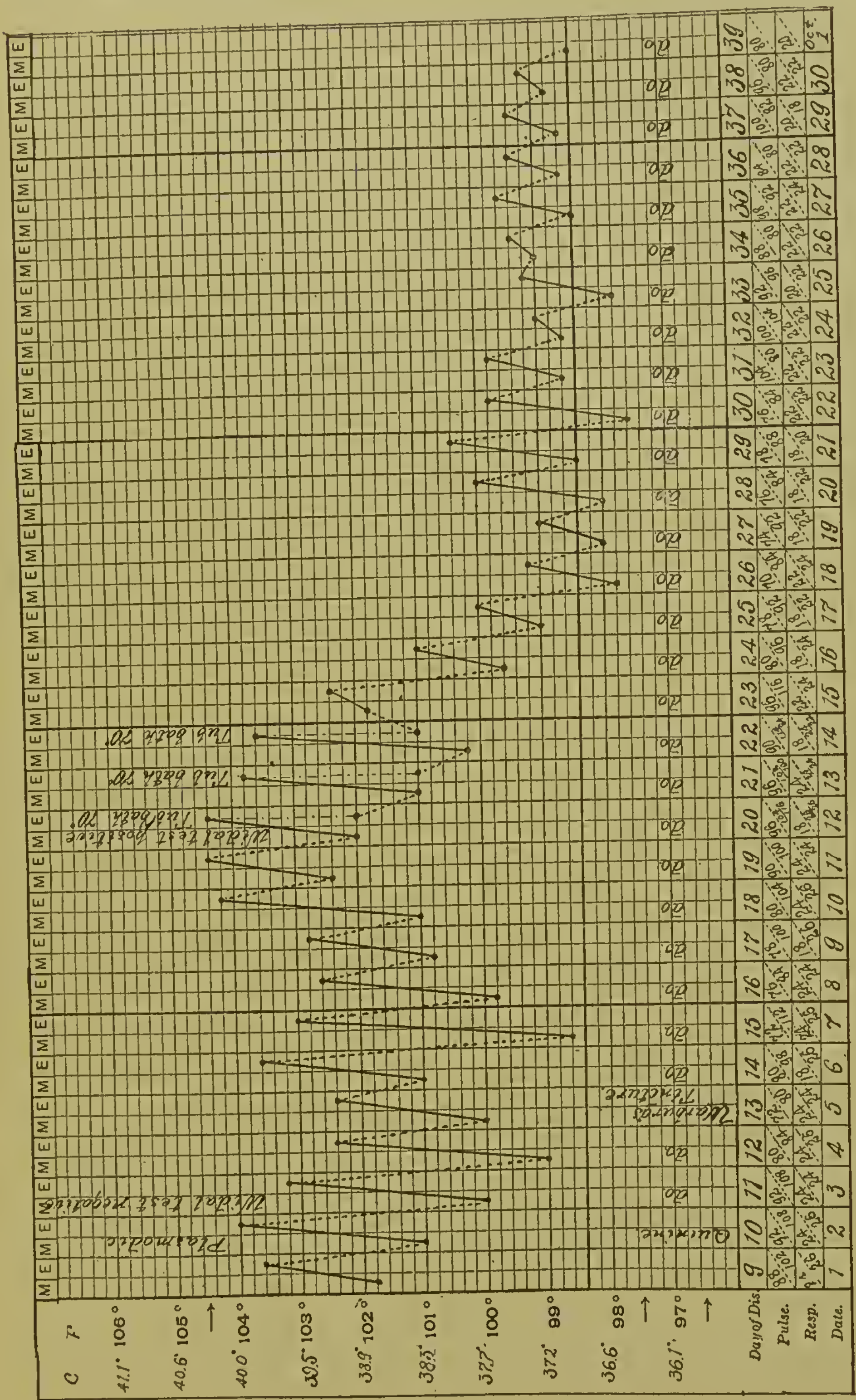

CHART No. 8.—Typhoid Fever Complicated with Malarial Fever. The dotted lines indicate the night temperatures.

was again obtained. The patient made an uninterrupted convalescence, though during the height of the fever he looked very sick and lost flesh rather rapidly. The Warburg's tincture was continued until he left the hospital on October 1st. No further malarial organisms were found nor were there any chills or other evidence of the malarial infection.

Cases such as the above would probably be more frequent were it not that the patient is rarely exposed to the two infections at the same time. The most recent studies of the mixed infection of typhoid fever and malaria have been made by Ewing at Camp Wikoff. They are of great interest and importance. Over two hundred cases of typhoid fever were studied and in nearly all of these there was also malarial infection. In five cases the plasmodium of malaria was found in the blood, but only during convalescence from the typhoid fever. From his observations, Ewing concludes that when typhoid develops in a case of active malaria, the malarial element nearly always becomes quiescent and has little or no effect on the course of the typhoid fever; also, that the malarial infection frequently outlasts the typhoid infection, and makes itself manifest during convalescence. It is probable that in my case related above the malarial manifestations were kept in check by the full doses of Warburg's tincture which were administered throughout the disease.

Varieties of Typhoid Fever.

Typhoid fever presents many variations in its course, and a large number of forms was described by the older writers. Many of these forms derive their names simply from some peculiarity in their mode of onset (pneumo-typhoid, nephro-typhoid), or from the presence of certain complications (thoracic form, hemorrhagic form), or from the predominance of certain symptoms (ataxic form, abdominal form, etc.). They do not represent any essential variation from the usual type of the disease and do not call for especial consideration. There are certain forms of typhoid fever, however, which differ so markedly from each other throughout their course that they may properly be called varieties of the disease. These varieties may be classified as follows: (1) The mild form; (2) the abortive form; (3) the afebrile form; (4) the latent or ambulatory form; (5) the acute or grave form. We may also consider with advantage typhoid fever as it occurs in children and in the aged.

The Mild Form.—Typhoid fever often appears in such a light and rudimentary form that its real nature is not recognized. These cases were formerly known as "gastric" or "bilious" fever. The usual

symptoms of typhoid fever are present but are only slightly developed. The spleen is enlarged, and rose-spots can generally be found if careful search is made. The fever is moderate and its duration seldom exceeds two weeks. It may, however, continue for the usual length of time. Griesinger was the first to demonstrate the enteric character of these cases and gave them the name of *typhus levissimus*. Often their diagnosis is most difficult and it may be impossible to establish it without question. Sometimes their specific nature is unsuspected until the occurrence of cases of undoubted typhoid fever in the same house or in the same neighborhood arrests our attention. The serum test of Widal promises to be a valuable aid in the diagnosis of such cases.

The Abortive Form.—In the abortive form of typhoid fever the disease begins like an ordinary attack with severe symptoms and high fever. Usually the onset is sudden, often being marked with a chill. The temperature rises rapidly, and enlargement of the spleen and rose-spots may be noted as early as the second or third day. Constipation is more frequent than diarrhœa, according to Murchison. Of eighty-seven cases observed by Jürgensen diarrhœa was present in only sixteen per cent. Early in the second week all the symptoms improve, the temperature becomes intermittent, and by the end of the second week the patient is convalescent. The temperature usually falls gradually, but sometimes the fever ends abruptly and with profuse perspiration. Liebermeister describes cases in which the temperature rose to 106° or even higher, and yet the total duration of the fever amounted to from seven to twelve days only. Griesinger has seen cases in which defervescence occurred as early as the fifth day. Osler is of the opinion that the abortive form of typhoid fever is not nearly so common in this country as in Europe.

The Afebrile Form.—This form of typhoid fever is extremely rare. Many physicians of large clinical experience have never met with a case. Murchison in his exhaustive work makes no reference to it whatever. Liebermeister was among the first to assert that typhoid fever sometimes ran its course without pyrexia. He cited cases which had come under his observation at Basle in which there were headache, malaise, furred tongue, loss of appetite, splenic enlargement, the characteristic rash, and in fact all the symptoms of typhoid except elevation of temperature. The pulse also was usually diminished rather than increased in frequency. Many of the patients were confined to their beds for four weeks or even longer. With convalescence the pulse increased, though the patients remained in bed. Liebermeister looked upon these cases as the result of a minimum infection, due to the widespread distribution of the typhoid poison

in Basle. Cayley also, in his Croonian lectures in 1880, refers to cases and even epidemics of typhoid fever in which the temperature was below normal throughout the whole course of the disease. As an instance of such an outbreak he cites the observations of Strube among the German soldiers during the siege of Paris in 1870. The epidemic broke out among the troops during the march to Paris and attained its greatest height in October. "In many of the cases the temperature was subnormal throughout and in others never exceeded the normal point. The roseola was usually profuse; the nervous symptoms were very severe and in inverse ratio to the temperature, consisting of violent delirium alternating with stupor; the duration of the fever was very short, defervescence usually taking place at the end of a fortnight. Of the twenty-three fatal cases, in twenty death took place during the first fourteen days. The abdominal symptoms were slight, but the characteristic lesions were found on post-mortem examination. All the cases were characterized by great prostration." The pulse was not diminished in frequency as in Liebermeister's cases; it was, however, but little accelerated, seldom exceeding 100. The tongue did not become dry and brown, and the enlargement of the spleen was either absent or less marked than usual. Strube attributed the peculiar features of this epidemic to the depressed condition of the troops; they had been exposed to great hardships on the way to Paris, overfatigued by forced marches and insufficiently supplied with food. In December a second outbreak occurred, when these conditions no longer prevailed, which resembled in every respect the ordinary form of typhoid fever.

In addition to the observations of Liebermeister and Strube, occasional instances of afebrile typhoid have been reported by different writers. The following case occurred in my service in Bellevue Hospital some five years ago, at a time when I was not familiar with the literature of the subject:

Daniel McFadden, aged 25 years, a salesman by occupation, entered the hospital August 6th, 1893. His family history was negative and the patient himself had had no previous illness with the exception of measles and whooping-cough in childhood. He had been a moderate drinker for four or five years. About one week previous to admission he began to feel weak and indisposed, with slight headache. He thinks he cannot hear quite so well as before. He has had no pain anywhere, but has a dull pressure in the small of the back. He had a diarrhœa for one day only, three days ago. Stools were watery but dark.

Upon admission (5 P.M.) the patient appeared fairly well nourished, but somewhat anæmic. The tongue was slightly coated and moist. The temperature was 100.6° and the pulse 116, regular and of fair

force. The thoracic and abdominal organs were apparently normal with the exception of slight enlargement of the spleen. No rash to be seen. The patient was put to bed and placed upon milk diet. Three days later, August 9th, a few rose-colored spots, disappearing on pressure, appeared upon the abdomen. General condition fair, but patient restless at night. On the following day the rose spots became more numerous and the diagnosis of typhoid fever seemed

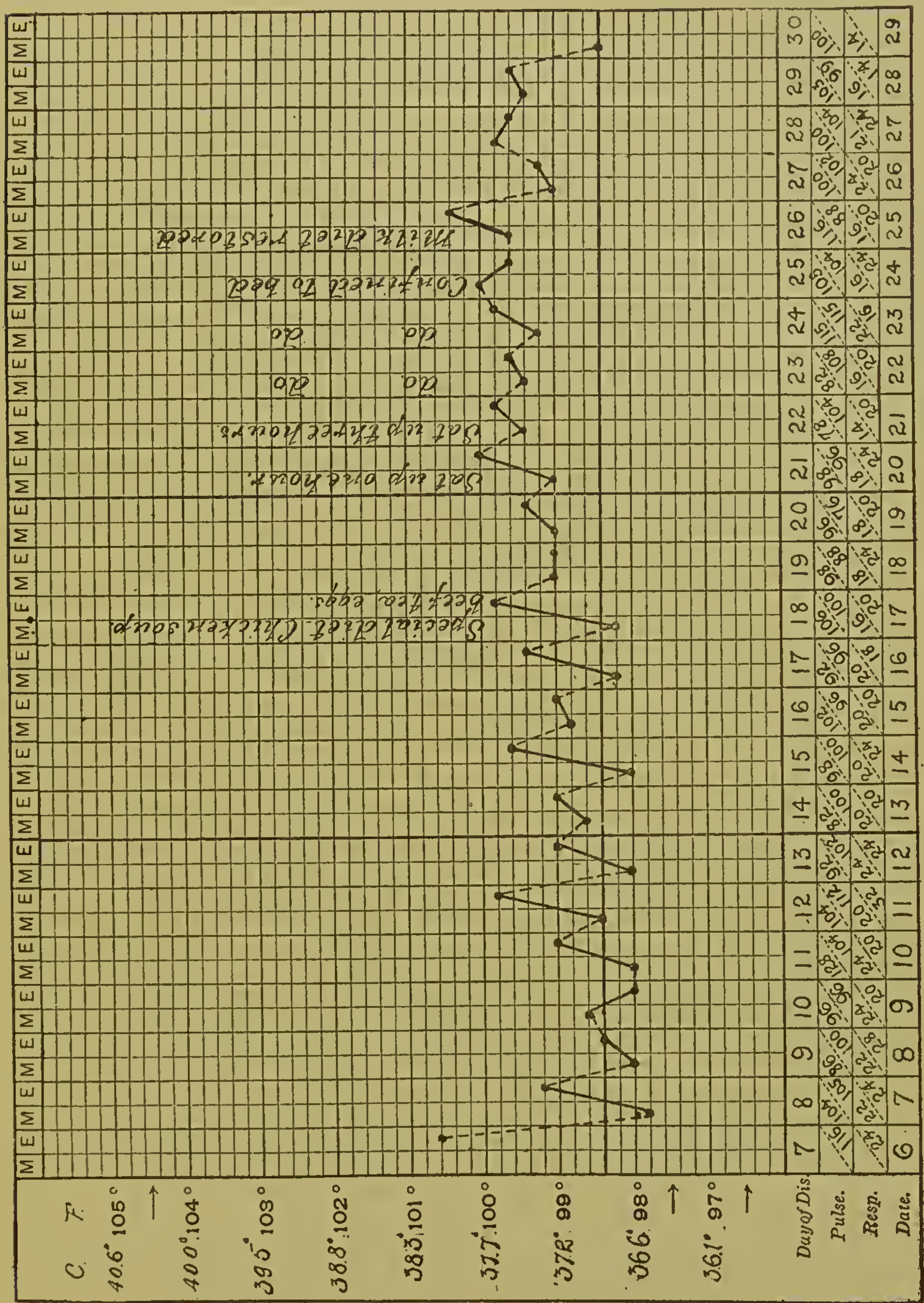

CHART No. 9.—Apyretic Typhoid Fever. The dotted lines indicate the night temperatures.

justified, in spite of the low range of the temperature, which had not been above 99.2° since the day of admission. The pulse, however, continued rapid, seldom falling below 100, and the patient looked sick. On the 13th, the pulse became dicrotic and the tongue tremulous and covered with a dry and brown coat, and prostration was marked. The bowels were constipated, requiring daily enemata. On the 17th, the patient's condition had much improved. His tongue had cleaned, though it was still slightly tremulous, and the pulse had lost its dicrotic quality. The temperature had continued low, falling in the morning to 98° and a fraction and rising in the evening to 99° and a fraction. The patient was now put upon special diet, consisting of chicken soup, beef tea, and eggs. He continued to do well, except that the temperature, as seen in Chart No. 9, rose a little, reaching 100° on the afternoon of September 20th, after the patient had sat up one hour. The pulse, on the other hand, was of good quality and somewhat slower in rate, and on the 21st and 22d the patient was allowed to sit up three hours each day. I noticed, however, as I looked at the patient in his chair, that he seemed very feeble and tremulous; the pulse also became rapid, being 115 both morning and evening on the 23d. I therefore confined him again to bed and on the 25th milk diet was restored, his temperature having risen on that day to 100.4°, the highest point since the day of entrance to the hospital. From this time on convalescence was uninterrupted, though the pulse rate continued rather high. During the first two weeks of the illness, the absence of fever had led me often to question whether this was really a case of typhoid. It was not until I saw the effect of giving solid food and allowing the patient to leave his bed that I felt sure of the diagnosis.

This case differs from those of Liebermiester and of Strube in that the pulse was unusually rapid rather than slow, and in the absence of the etiological factors of overfatigue and insufficient food.

The Latent or Ambulatory Form.—In this form, often called "walking typhoid," the symptoms are usually so slight that the patient does not feel ill enough to go to bed or to consult a physician. He is conscious of malaise and feverishness, but he is able to keep on his feet and in some cases attend to his ordinary affairs. If the type of disease is mild, it may pass through its course unrecognized. More often, however, the illness is interrupted and its nature revealed by the occurrence of some alarming symptom, such as acute delirium, intestinal hemorrhage, or perforation of the bowel. The last is said by Murchison to be the most common accident in these cases, "the walking about of the patient being calculated to rupture the denuded peritoneum forming the base of the intestinal ulcers." Sometimes the patient comes by chance under the observation of a physician and the disease is recognized before any accident has occurred. James C. Hutchinson, in his article on typhoid fever in Pepper's "American System of Medicine," relates his own case as an instance of

this kind. Supposing that the excessive prostration from which he was suffering was due to overwork at a large army hospital in the neighborhood of Philadelphia, he determined to seek repose in travel and in change of scene. On the eve of doing so he fortunately sent for a medical friend, who, after a thorough investigation of his symptoms, succeeded in finding a few rose-colored spots upon his abdomen. The attack subsequently ran a mild but well-marked course.

The severer forms of latent typhoid fever are usually seen in workingmen, such as farm laborers, longshoremen, and sailors, men accustomed to pay but little attention to their own symptoms and also obliged by necessity to keep at work as long as possible. "Walking typhoid" with fatal result is a rare occurrence among the well-to-do classes, although the other forms of the disease are quite as frequent among the rich as among the poor.

The Acute Form.—In the acute or grave form of typhoid fever the disease sets in suddenly and with great violence. The attack usually begins with intense headache, quickly followed by acute delirium and high fever. Often, particularly in children, there is vomiting followed by diarrhœa. There is generally a marked tendency to early pulmonary complications, such as lobar pneumonia and congestion of the lungs. These cases are usually rapidly fatal, and death may occur in the first week and even as early as the second day. On autopsy the characteristic early lesions are found in the bowel, as well as marked enlargement of the mesenteric glands.

Fortunately this fulminating form of typhoid fever is very rare, most observers recording but one or two cases in their experience. The following case, taken from Murchison, is a good illustration of this variety of the disease:

In June, 1861, a girl, aged 9 years, was admitted into the Middlesex Hospital. The girl had been quite well the day before admission, when she had been suddenly seized with vomiting and febrile symptoms, followed by severe purging, intense headache, and acute delirium, which symptoms continued until death, forty-seven hours from the beginning of her illness. On autopsy, the solitary glands and Peyer's patches in the ileum and colon were much enlarged and contained a yellowish-white morbid material. There was no ulceration. The mesenteric glands were as large as hazelnuts and congested.

Typhoid Fever in Infancy and Childhood.

Typhoid fever is rare in infancy but not uncommon in childhood. It was formerly generally believed that children were not subject to the disease, although they were known to be very liable to a fever at-

tended with gastric and intestinal symptoms, and usually termed "infantile remittent fever." It was not until 1840 that Rilliet and Taupin showed, independently of each other, that the majority of cases of infantile remittent fever were really instances of typhoid fever. Further observations have confirmed this view, and it is now known that children are particularly susceptible to typhoid fever and are often attacked, as Murchison observes, when other members of the family escape. Even infants have been known to take the disease. The youngest case on record, according to Crozer Griffith, is that reported by Gerhardt, a child of three weeks born of a typhoid mother and kept in the same room with her. Osler states that perforation has been met with in an infant five days old, but this case should perhaps be considered an instance of fœtal typhoid. Ogle reports a case in a child of four and one-half months, and Crozer Griffith describes two cases in children of three and seven months respectively. The latter writer refers to these and other cases, and is of the opinion that typhoid fever in infants is far more common than is generally believed, and that our failure to recognize it is partly due to the fact that we have not sought for it at this early age, and in part because the symptoms at that time are not so characteristic. Holt, on the other hand, who has never seen typhoid fever in a child under two years of age, believes that it is very rare in infancy and calls attention to what is undoubtedly the fact, that the reported cases in infants have almost invariably been observed in general epidemics. Morse and Thayer, also, as a result of some recent observations, indorse the commonly accepted view that typhoid fever is an unusual disease in infancy. They applied the Widal test to the blood of 50 babies under two years of age, with the following clinical diagnosis: Simple diarrhœa, 2 cases; fermental diarrhœa, 45 cases; ileocolitis, 3 cases. In only one case was a positive serum reaction obtained, and a test of the blood of the mother of this patient gave a positive reaction in fifteen minutes. The mother had had a slow fever ten years before, but had not been ill since. The child had been taken sick when seven months old with greenish diarrhœa and vomiting. The treatment began four days after the beginning of the attack, and in nine days the child was entirely well. Under the circumstances it seemed probable that this case was not one of typhoid fever. After the second year the frequency of the disease in children increases up to the age of ten or twelve years and then declines. The relative frequency at different ages is fairly represented by the following figures obtained by combining the experience of Henoch in private and hospital practice in Berlin and that of Schavoir in the Stamford epidemic: Of 331 cases under the age of fifteen years, 101 were under

five years, 135 were between five and ten years, and 95 were between ten and fifteen years.

Typhoid fever in children is usually of mild type and short duration as compared with the same disease in adults. The onset is more often sudden than in older persons, though cases with slow and insidious onset are also frequent. The cases with abrupt onset resemble the abortive attacks in adults, in the rapid development of the characteristic symptoms as well as in the quick decline of the fever. Vomiting is a frequent initial symptom, as in the other acute infectious diseases of childhood. Holt has once known the disease to be ushered in by convulsions, but this is very exceptional. An initial chill is rare. Henoch observed it in a few of his cases, and once at the beginning of a relapse. Epistaxis is less frequent than in adults. The average duration of the fever is from two to three weeks. Of eighty cases observed by Henoch, in which the duration could be accurately calculated, in twenty defervescence took place between the seventh and twelfth days. In only twelve was the course protracted beyond three weeks. The temperature curve is less regular than in adults. The initial rise is more rapid, as a rule. During the height of the disease the temperature often remains high, with but little variation between the morning and evening elevations (Crozer Griffith). During the second week the remittent character of the fever is less marked than in adults. According to Morse's figures it is absent altogether in about half of the cases. This is in agreement with the fact that the intestinal lesions in children are less extensive and usually undergo resolution without ulceration. The range of the temperature is usually somewhat higher than in cases of like severity in adult life. All observers agree, however, that children bear high temperatures much better than older persons. Liebermeister states that the only case which he saw recover after the temperature had risen repeatedly to 107.5° occurred in a girl fourteen years of age. Crozer Griffith also relates the case of a girl ten years old, characterized by hyperpyrexia, the temperature on one occasion reaching 107°, and for over two days being much of the time above 106°. The mind, however, remained entirely clear, the nervous system was apparently in a perfectly normal condition, and the child was bright and cheerful. The patient made a good recovery.

The eruption is said by most observers to be less constant and less abundant in children than in adults. Of 670 cases in Morse's series, the rash was found in but 406, or 60 per cent. Crozer Griffith, on the other hand, agrees with Baginsky that the rash is seldom absent. In many cases it is probably present at some time during the attack, but is overlooked. Enlargement of the spleen is more

constant than in adults. According to Crozer Griffith it is always present, although not always discoverable. I have, however, recently seen a case in a child of six years, in Bellevue Hospital, in which careful daily examination failed to reveal either rash or enlargement of the spleen, although the abdomen was soft, permitting free palpation beneath the ribs. The child died during the height of the fever, and on autopsy swelling of Peyer's patches with slight superficial ulceration was found, as well as marked enlargement of the mesenteric glands, but the spleen was of normal size. The Widal reaction had been positive in the dilution of 1 : 20. Henoch also refers to cases in which the characteristic temperature curve was the only symptom present, diarrhœa, eruption, and enlargment of the spleen all being absent.

The nervous symptoms in children, although more prominent than the intestinal symptoms, are nevertheless much less severe, as a rule, than in adults. Many children, as Henoch observes, sit up in bed, smile, and even show some appetite, although the elevation of temperature may be considerable. Headache is common, especially at the beginning of the disease, and there is usually more or less apathy. There is often mild delirium, and in very young children there may be violent screaming at night. The older the children the more inclined they are to severe nervous disturbances, but even in them the symptoms of the typhoid state, such as subsultus, stupor, coma vigil, and coma, are rarely seen. Sometimes a condition closely resembling meningitis is observed. The intestinal symptoms are seldom of great intensity. In children under ten years of age constipation appears to be more frequent than diarrhœa. Diarrhœa when present is rarely profuse. Intestinal hemorrhage is rare, particularly in young children. Of 553 cases of typhoid fever in children, collected by Morse, hemorrhage occurred in only 9, or 1.6 per cent., and these were all in children over ten years old. Serious complications and sequelæ are less frequent in infancy and childhood than in adult life. Perforation of the bowel is even more rare than hemorrhage. Henoch saw it but once in all his experience, and then it occurred in the fifth week after convalescence had begun. In 1,028 cases collected by Holt, perforation took place only 12 times, or in a fraction over 1 per cent. The rarity of both hemorrhage and perforation in children is explained by the slight development of the intestinal lesions and the absence of ulceration. Slight albuminuria is not uncommon during the height of the fever in severe cases, but nephritis is seldom seen. Meningitis is extremely rare. Among the sequelæ, otitis, aphasia, and lesions of the bones are more frequent in children than in adults. According to Holt, otitis is seen principally in young

children and during the cold season. Aphasia is usually temporary. In two of twenty-one cases collected by Morse it was due to embolism; in the remainder it was apparently not dependent upon any organic lesion. In nearly all the cases complete recovery occurred after an average duration of three weeks.

The mortality of typhoid fever in children is low. Of 2,623 cases collected by Holt from the reports of twelve different writers, the mortality was 5.4 per cent. Holt observes, moreover, that these are almost all taken from hospital reports, where, as a rule, the mildest cases are not brought for treatment. In his opinion, the mortality of the disease in children, including all cases, does not exceed three or four per cent.

Typhoid Fever in the Aged.

Typhoid fever is comparatively rare in persons over fifty years of age. It occasionally occurs, however, at very advanced ages. Of 5,911 cases at the London Fever Hospital, 27 patients were over 60 years of age and two above 75. Trousseau observed a case in a patient 64 years of age, Wilks one at 70, Lombard one at 72, Heulard d'Arcy one at 86, Hamernyck one at 90, and Gueneau de Mussy one at 100 years of age.

The onset of typhoid fever in persons beyond middle age is even more gradual and more insidious than in early life. Headache is rarely severe and is often absent entirely. The temperature is usually but little elevated even during the height of the disease. Subnormal temperatures are frequently observed, especially in convalescence. The eruption is scanty and is often wanting. The spleen is but slightly enlarged or is apparently normal in size. The abdominal symptoms are seldom pronounced, though intestinal hemorrhage and perforation sometimes occur. Pulmonary complications, on the other hand, are frequent, especially hypostatic congestion and pneumonia. The most marked feature of typhoid fever in the aged is the extreme debility which characterizes the disease from the beginning. This is the more noticeable because of the apparent mildness of the course of the fever. Convalescence is slow and uncertain.

The diagnosis is often difficult, particularly in the atypical cases and in those with pronounced pulmonary complications. It is probable that the true character of the disease is frequently not recognized, as in the two cases reported by Osler which had been regarded as instances of senile pneumonia until the autopsy showed the presence of typhoid ulcers in the bowel. The mortality is very high, ranging from thirty (Liebermeister) to fifty per cent. (Uhle). Failure of the heart is a frequent cause of death.

DIAGNOSIS.

The diagnosis of typhoid fever may be very easy or it may be extremely difficult or even impossible. The peculiar range of the temperature, the characteristic eruption, and the enlargement of the spleen are the most distinctive symptoms. In private practice cases usually come under observation towards the middle or end of the first week, in hospital practice seldom before the eighth or tenth day of the disease. Even during the first week in typical cases a probable diagnosis can often be made from the history of gradual onset and steadily ascending temperature, attended with headache, malaise, and perhaps epistaxis. Enlargement of the spleen takes place in typhoid fever by the end of the first week and, if detected, is a most important sign. Although, as Osler observes, it occurs in other febrile conditions, it nevertheless establishes the fact that we have to do with an infection and not simply a "bilious attack" or a febricula. The diazo reaction of the urine is also of considerable value at this period of the disease. Early in the second week the rash usually appears and with the other symptoms establishes the diagnosis. It is well, however, to remember the rule not to make a diagnosis of typhoid after a single examination of the patient. Indeed, it is necessary to watch the case for some time in order to obtain the characteristic temperature curve. If the patient is first seen during the second week or later in the disease, the course of the fever is still the most important factor in the diagnosis, especially in the absence of the rash or evident enlargement of the spleen. At this time, however, we have usually the typhoid facies, as well as the hebetude and prostration of the patient to aid us in forming our diagnosis. The absence of any local lesion of sufficient intensity to account for the symptoms is also of value as negative evidence.

The atypical varieties of typhoid are those which cause the greatest difficulty of diagnosis. The very mild cases, in which the fever is slight or altogether absent, may leave us in doubt until the very end of the disease. In such cases the presence of undoubted cases of typhoid fever in the immediate neighborhood is an important factor in diagnosis. The abortive cases beginning with chill and abrupt rise of temperature are often misleading at the outset. In the aged the irregular course of the disease renders the diagnosis very difficult, and in some cases the real nature of the disease is not suspected until the autopsy shows the intestinal lesions of typhoid. The differential diagnosis from those acute diseases that most resemble typhoid fever will be considered presently.

Serum Diagnosis.—In June, 1896, Widal proposed and described a new method of diagnosticating typhoid fever by means of an examination of the blood or serum. This "serum test" was the outcome of a long series of experiments in immunization which had been carried on simultaneously by observers in France, Germany, and England. The importance of the subject demands a short account of the studies which paved the way for the discovery of Widal.

Chantemesse and Widal were among the first experimenters in this field. In 1888 they succeeded in immunizing animals against the typhoid bacillus by injecting them with sterilized cultures of that bacillus. These observers found later (in 1892) that the same result could be accomplished by means of the serum of patients suffering from typhoid fever or convalescing from that disease. Then followed the observations of Pfeiffer and Kolle, who showed that the serum of typhoid convalescents or the serum of immunized animals, when injected into the peritoneal cavity of guinea-pigs at the same time with a virulent culture of the typhoid bacillus, had the property of immobilizing, agglutinating, and rapidly disintegrating the bacilli in the serous fluid. This reaction is generally known as "Pfeiffer's phenomenon" or reaction. The same serum, injected in like manner with cultures of the colon bacillus, had no such effect, the bacilli remaining isolated and motile. Later, Gruber and Durham observed the same immobilizing and agglutinating action upon typhoid bacilli outside the animal body, the mixture being made *in vitro*. There was no action upon the colon bacillus in any of its varieties. Again, Pfeiffer and Kolle showed that if the serum of immunized animals was added to bouillon in certain proportions, and the bouillon was then sown with typhoid bacilli, there resulted after twenty-four hours a clear fluid with the bacilli precipitated at the bottom of the tube collected into small clumps. Colon bacilli, sown in the same bouillon, caused the usual clouding and preserved their motility. Pfeiffer and Kolle therefore recommended this procedure as a means of distinguishing between the typhoid and the colon bacilli. Widal carried these last observations one step farther, and found that the serum of typhoid patients had on cultures of the typhoid bacillus the same agglutinating action as the serum of animals immunized against typhoid fever. The serum of healthy individuals, on the other hand, or of persons suffering from diseases other than typhoid fever, had no such property. Having arrived at this point, Widal had only to reverse the terms of the problem and ascertain how the blood serum of a given individual acted upon a culture of the typhoid bacillus. If the addition of the serum produced immobilization and clumping of the bacilli in the culture, the individual had typhoid fever or had

recently recovered from the disease. If the bacilli were unaffected, typhoid fever could be excluded.

Since Widal first proposed the serum test it has been demonstrated that the agglutinating substances in the blood which cause the typhoid reaction are also sometimes present in small amount in other diseases and even in health. A slight or pseudo-reaction may, therefore, occasionally occur in cases non-typhoid in nature, if a large amount of serum is taken. The question of the proper dilution of the serum is all-important. There are various ways of performing the test, but the principle is the same in all. As already indicated, the test consists in adding human blood or serum in certain proportions to a recent culture of the typhoid bacillus, and noting the effect upon the motility and arrangement of the bacilli in the mixed fluid. The following method, perfected by Biggs and Park, is employed in the Health Department of New York City: One part of blood or serum is added to ten parts of a twenty-four-hour bouillon culture of the typhoid bacillus, and a drop of the mixture is examined at once under the microscope. If the movements of the bacilli are unaffected, the result of the test is negative. When the typhoid reaction appears, the bacilli quickly lose their motility and become clumped together in masses. If the reaction occurs promptly with a dilution of 1:10, it is concluded that the patient in all probability has typhoid fever, or has had it within one year. The dilution is then increased, and if a marked reaction takes place when one part of blood or serum is added to twenty parts of bouillon culture, the probability that the patient has typhoid fever becomes almost a certainty.

Either dried blood or serum obtained from a blister may be used for the test. The serum can be more accurately diluted than the blood and is therefore preferred for examination, but in practice the dried blood has been found to answer all the purposes of the test. The blood may be taken from the lobe of the ear or the tip of the finger, the usual antiseptic precautions being observed. Two or three drops of blood are placed upon a clean glass slide and allowed to dry. The slide is then forwarded to the laboratory, where the dried blood is dissolved by adding one or more drops of distilled water until the desired dilution is obtained.

The serum test has been thoroughly tried during the past three years and its value as well as its limitations are now well defined. There is no doubt that the test is a most valuable addition to our means of diagnosis. It is, however, not an infallible sign, nor is it always an early sign of the disease. On collecting the published reports of a large number of observers it appears that the results of the test are in accord with the clinical diagnosis in about ninety-five per

cent. of the cases. In about five per cent. of the cases the blood does not respond to the test at any time in the course of the disease. The absence of the reaction in any individual case does not, therefore, positively exclude the diagnosis of typhoid fever. The time of appearance of the reaction is very important. Often it is not present until the diagnosis has already been made from the clinical symptoms of the disease. According to Biggs, the blood or serum of typhoid patients gives the reaction during the first week in about 70 per cent.; during the second week in about 80 per cent.; and during the third and fourth weeks in about 90 per cent. of the cases. Tuttle reports that of 31 cases in the Presbyterian Hospital in which the time of the first appearance of the reaction was noted, 16, or 52 per cent., reacted during the first week of the disease. Osler's experience is less favorable. In a series of 108 cases in the Johns Hopkins Hospital the reaction was present before the seventh day in only 26 cases. A negative reaction is of less significance than a positive result, especially if the examination is made during the early days of the disease. In such cases the test should always be repeated during the following days; the reëxamination is a most important part of the test. There are many cases in which the reaction is absent during the first week but appears during the second or third week of the disease. Occasionally the peculiar property of the blood upon which the test depends is not developed until convalescence has been established. In March, 1897, I reported a case of typhoid fever in which the reaction continued negative until the fifth week of the disease. Two weeks later a positive reaction was given by the fluid from a blister, the patient being apparently convalescent. The blood serum, however, still failed to react. One week later the patient had a relapse, and a reaction was obtained from both blood serum and blister fluid. In this case the test could not be said to be an aid to diagnosis; in fact the negative result was absolutely misleading. Such cases, however, are very exceptional. On the other hand, a positive reaction is sometimes obtained in diseases other than typhoid fever, but probably not oftener than in one or two per cent. of the cases. Even this percentage will diminish if the serum is diluted sufficiently. The experiments of Stern and others have shown that a dilution of 1:50 entirely removes the danger of observing a normal or pseudo-reaction. It should always be borne in mind that the serum reaction is a quantitative rather than a qualitative test.

Isolation of the Typhoid Bacilli from the Stools and Urine.—As has already been stated, His has succeeded in isolating the specific bacilli from the stools of about ninety per cent. of cases carefully investigated during the febrile stage. Several cases in which no Widal reaction

was demonstrated gave positive results, and in one case the bacilli were found on the first trial on the tenth day of the disease, three examinations for the Widal reaction having proved negative.

The bacilli are found with less frequency in the urine than in the fæces, but still often enough to show that the investigation of the urine is of great importance. The fact that they have been isolated from the urine as early as the third day of the disease emphasizes the value of the proceeding from a diagnostic standpoint.

Diseases Liable to be Confounded with Typhoid Fever.—The diseases which most frequently cause difficulty in diagnosis are typhus fever, influenza, simple continued fever, acute general miliary tuberculosis, tuberculous meningitis, tuberculous peritonitis, malarial fever, cerebrospinal meningitis, acute pneumonia, pyæmia, malignant endocarditis, and appendicitis.

Typhus fever is distinguished from typhoid fever by its sudden onset, the early and profound prostration, the dusky face with swollen eyelids and injected conjunctivæ, and the early appearance and character of the rash. The eruption is more constant and much more abundant than in typhoid and usually appears on the fourth or fifth day of the disease. It is in the form of pinkish macules, rapidly growing darker and often, but by no means always, becoming petechial early in the second week. The duration of the disease is short and it terminates abruptly by crisis, usually on or about the fourteenth day. The distinction between the two diseases is, however, not always so clear-cut as the above description would imply, and in all epidemics there are cases in which, in the absence of a history of exposure, it is difficult to decide whether typhus or typhoid fever is present.

Errors of diagnosis are most apt to occur in cases in which the typhus eruption is slight or the typhoid eruption is profuse. Doty, in his admirable article on typhus fever in the "American System of Practical Medicine," states that he has seen numerous cases of typhoid which had been positively declared to be typhus fever on account of the accompanying general eruption. In some cases it was a profuse typhoid eruption; in others it was a septic eruption or an accidental one. Two such cases have come under my observation. One of them is now convalescing in the Reception Hospital of the Health Department. Both cases were sent to the hospital to be isolated, not because the disease was believed to be typhus fever, but because the unusually profuse eruption suggested the possibility of a typhus infection. In both cases the eruption covered the entire body and there were numerous spots which did not disappear on pressure. These spots were, as a rule, caused by the bites of pediculi with which the clothing of the patients was infested. In neither case could a his-

tory of the period of invasion be obtained. In the case now under observation the face was dusky, the skin congested, the conjunctivæ were injected, and the patient was delirious at the time of entrance into the hospital. Had there been an epidemic of typhus fever in the city at the time, the probability of a typhus infection would have been strong.

Influenza, especially of the gastro-intestinal type, may be confounded with typhoid fever. The disease may set in with headache, fever, diarrhœa, and abdominal pain and tenderness. The spleen may also be enlarged, though, as a rule, not to the extent observed in typhoid. The abruptness of the onset, the early and profound prostration, and the multiplicity of symptoms, so characteristic of influenza, aid us in differentiating this disease from typhoid fever. On the other hand, the nervous form of typhoid sometimes resembles influenza very strongly during the first few days. Ultimately the course of the disease and particularly the continuance of the fever render the diagnosis clear.

Simple continued fever can usually be distinguished from typhoid by the absence of prodromes, by the abrupt rise of the temperature, and by the presence of constipation rather than diarrhœa. Moreover, as observed by Da Costa, whatever doubt may exist is cleared up in a few days, as the symptoms in simple continued fever come to an end at a time at which in typhoid fever they begin to be more and more developed.

Acute general miliary tuberculosis may readily be mistaken for typhoid fever. The differential diagnosis between the two affections is often extremely difficult. In both the onset is gradual, with loss of appetite, cough, and steadily increasing fever. Bronchitis is common to both diseases. Diarrhœa and tympanites are rare in tuberculosis; the abdomen is usually retracted and the bowels are constipated. But diarrhœa may occur and persist for days, and in certain cases the diagnosis has been complicated still further by the appearance of blood in the stools (Osler). The chief point of distinction is the irregularity of the temperature curve in acute tuberculosis. The respiration also is more rapid than in typhoid fever, even though no extensive pulmonary lesion can be detected. Enlargement of the spleen, though usually present, is also less marked than in typhoid. The absence of the characteristic rose rash is an important element in diagnosis, though in rare instances an eruption appears which is distinguished with difficulty from that of typhoid fever. Murchison describes a case in which from the fourth day until death there were successive crops of circular reddish spots which disappeared on pressure. They differed, however, from those of typhoid fever in their early appearance, and in the long period over which they kept com-

ing out. Still, during life, the case was regarded as one of enteric fever. The patient died, and on autopsy there was no sign of ulceration in the ileum, but the lungs, liver, spleen, kidneys, and peritoneum were studded with miliary tubercles.

Acute tuberculous meningitis is not often confounded with typhoid fever, but may occasionally cause difficulty in diagnosis. In both diseases the onset may be characterized by headache, vomiting, fever, and delirium. In meningitis, however, the headache is more intense, the vomiting more urgent, and the delirium more active than in typhoid. This is particularly true of children in whom tuberculous meningitis is more apt to occur than in adults. The temperature also is extremely irregular, and the pulse, at first rapid, becomes slow and irregular. Ophthalmoscopic examination of the eyes will often show tubercles in the choroid.

Tuberculous peritonitis, when of gradual onset, may be mistaken for typhoid fever. The abdominal tenderness is, however, more persistent than in typhoid and more widely diffused. The temperature is irregular and at times subnormal. Leucocytosis also is present in this as in the other forms of tuberculosis, but is absent in typhoid.

Malarial fever and typhoid fever are not infrequently mistaken for each other. This is particularly true in regions where both fevers are common. The remittent form of malarial fever offers the greatest resemblance to typhoid fever. The fever may be almost continuous, with remissions similar to those of typhoid. Chills may be absent, the spleen is enlarged, and there may be an initial bronchitis. The absence of the rose rash is an aid to correct diagnosis and the fever yields, as a rule, readily to quinine or to Warburg's tincture. The examination of the blood, however, offers the most certain means of diagnosis. The malarial parasites are usually to be found without much difficulty, though sometimes, as observed by Osler, the æstivo-autumnal variety may not be present in the circulating blood for several days. Typhoid fever, on the other hand, may easily be mistaken for malarial fever, especially in the first few days of the disease. The gradual onset and the absence of paroxysmal chills usually enable us to exclude malarial infection. Chills and sweating are sometimes met with in typhoid, as in the cases described by Osler, but they do not occur with the regularity characteristic of malarial fever. Nevertheless, the blood examination may be necessary in order to make a positive diagnosis. The absence of the malarial parasites and the presence of the Widal reaction leave no further room for doubt. Reference has already been made to the occasional occurrence of typhoid fever and malarial fever in the same patient.

The cerebral form of typhoid fever may simulate *cerebrospinal*

meningitis very closely. The disease may set in suddenly with severe headache, delirium, retraction of the head, and twitching of the muscles, and it may be impossible to make a certain diagnosis until the appearance of the rash. Osler states that he has "thrice performed autopsies on cases of this kind in which no suspicion of typhoid fever had been present, the intense cerebrospinal manifestations having dominated the scene." Such cases are, however, very rare. Here again the examination of the blood may determine the diagnosis. In cerebrospinal meningitis there is usually leucocytosis, whereas in typhoid fever the blood reacts to the Widal test. The rarity of cerebrospinal meningitis and the frequency of typhoid fever should also be borne in mind.

Acute lobar pneumonia may be confounded with typhoid fever. Cases of typhoid fever setting in with a chill and marked pulmonary symptoms may readily be taken for cases of simple primary pneumonia. As the disease progresses the characteristic signs of typhoid appear and the symptoms of the local lesion fall into the background. Osler states that he has brought such a case before the class one week as typical pneumonia and a fortnight later shown the same case as undoubtedly one of typhoid fever. On the other hand, there are cases of pneumonia in which severe secondary symptoms develop, resembling the typhoid state, so that it may be impossible to exclude typhoid fever with certainty. Such cases are particularly apt to occur in elderly people and we may be in doubt whether we have to do with senile pneumonia or with the so-called pneumotyphus.

Pyæmia is sometimes mistaken for typhoid fever, especially when the focus of infection is deep-seated. Fagge observed two cases at Guy's Hospital in which such a mistake was made. In each of them the source of the infection was latent disease of the lumbar or the dorsal vertebræ, there being secondary abscesses in the lungs and the kidneys, and once in the heart. As a rule, the temperature in pyæmia is more irregular, and the chills and profuse sweatings serve to distinguish it from typhoid. Sometimes, however, as observed by Osler, chills and sweats may be absent. In such cases the presence of leucocytosis is a valuable diagnostic sign, especially when taken in connection with the absence of the Widal reaction.

Malignant endocarditis often strongly resembles typhoid fever. In both diseases there are diarrhœa and abdominal tenderness and enlargement of the spleen. In both there are delirium and stupor and progressive exhaustion. In endocarditis the onset is more abrupt, and the fever is less regular in type than in typhoid. There is usually cardiac distress, though sometimes the cardiac symptoms, both subjective and objective, are entirely wanting. Leucocytosis is

marked in malignant endocarditis, but is absent in typhoid fever, unless inflammatory complications occur.

Appendicitis and typhoid fever are sometimes mistaken for each other. Such a mistake is usually soon detected, as the local symptoms in the one case and the constitutional symptoms in the other establish the diagnosis within a few days. The onset in appendicitis is more abrupt and the pain and tenderness in the right iliac region are more acute than in typhoid. In place of gurgling in this region there is a sense of resistance on palpation as well as dulness on percussion. Often a clearly defined tumor can be made out as the inflammatory process progresses.

Prognosis.

The prognosis in typhoid fever should always be guarded. The disease may apparently be of a very mild type and progressing favorably when suddenly the whole aspect of the case is changed by the occurrence of some complication, such as profuse hemorrhage or perforation of the intestine. On the other hand, recovery sometimes takes place when the case has seemed hopeless. The prognosis depends largely upon the period of the disease at which the case comes under the care of a physician. The earlier in the attack the patient is put to bed, the more favorable the prognosis. Cases of "walking typhoid" in which the patient has kept about for a week or more are particularly apt to terminate fatally. The most important unfavorable symptoms are continuous high temperature, rapid pulse (120 and over), low muttering delirium, meteorism, intestinal hemorrhage, and the signs of perforative peritonitis. The significance of these symptoms has already been dwelt upon in previous sections and need not be repeated here. Severe muscular tremor is also a serious symptom, as it is believed to indicate deep and rapid ulceration of the bowel. Typhoid fever is more fatal among women than among men. The difference in mortality, however, is but slight, not over one per cent. Pregnancy is a serious complication, but not so grave as was formerly supposed. Abortion occurs in the majority of cases, but the patient usually recovers. The prognosis is unfavorable in very fat persons as well as in those who have been intemperate. It is also grave, according to Murchison, in gouty subjects and in those who have disease of the kidneys. In children under fifteen the prognosis is very favorable, as has already been stated.

Sudden death sometimes occurs in typhoid fever without premonitory symptoms and without evident organic cause. It may take place during the height of the fever or even during the course of an appar-

ently normal convalescence. Only one instance has come under my observation. It occurred in a young woman who was convalescent from a moderately severe attack of typhoid. The attending physician had ceased his visits, and the patient at the time the accident took place was alone in her room and was preparing to join the family at dinner. They heard a cry from her room and found her lying helpless on the bed. She gasped a few words of explanation, and when I reached the house some ten minutes later she was dead. The attending physician who arrived soon after said that the patient had shown no signs of cardiac weakness at any time in her illness. It is possible, however, that there may have been an inherited weakness of the heart in her case. Her death occurred about ten years ago, and since that time other members of her family have at times suffered from marked irregularity of the heart, which is liable to come on under any mental or physical strain. Sudden death is much more frequent in men than in women, in the proportion of 114 to 26, according to Dewèvre's statistics.

The mortality in typhoid fever is very variable. Previous to the introduction of the Brand method of treatment, the death rate in hospitals ranged from 12 to 25 per cent., with an average mortality of about 17 per cent. A remarkable exception to this high rate is afforded by the Cork Street Fever Hospital, Dublin, in which, during the twenty years ending March 31st, 1891, 1,405 cases of enteric fever were treated, of which only 121 proved fatal, or 8.6 per cent. The mortality in private practice is, for obvious reasons, considerably less than that in hospitals. It is difficult to obtain accurate statistics on any large scale, but the death rate is estimated to be about ten per cent., varying with the severity of different epidemics. In the epidemic at Plymouth, Pa., in the summer of 1885, 1,200 persons were attacked, and 130—or 10.8 per cent.—died. The mortality was even less in the epidemic at Maidstone, England, in the autumn of 1897, the total deaths being 143 out of 1,886 cases, or only 7.6 per cent. Under the use of cold baths the death rate in hospitals has been greatly reduced, so that now it does not differ materially from that in private practice, being about 7.5 per cent. in those institutions in which the Brand method is strictly carried out. Those hospitals which adhere to the expectant plan of treatment, such as the Metropolitan Fever Hospital and the Monsall Fever Hospital, still show a high rate of mortality, it being about 17 per cent. in the former and 17.18 per cent. in the latter institution. Osler states that the last report of the British Army Medical Department (1896) shows an increase in both incidence and mortality.

The following table, compiled in the office of Surgeon-General

Sternberg, gives the annual number of cases and mortality in the United States army for the ten years ending with June, 1898:

Year.	Cases.	Deaths.	Percentage. Deaths to cases.	Year.	Cases.	Deaths.	Percentage. Deaths to cases.
1888.........	80	13	16	1894........	152	20	13
1889.........	133	15	11	1895........	109	13	12
1890.........	127	13	10	1896........	148	17	11
1891.........	92	12	13	1897........	159	9	6
1892.........	144	13	9				
1893.........	159	16	10	Total.....	1,303	141	10.8

The returns for the year just past in our army, in so far as they are now available, are even more favorable than the above. During the summer and autumn of 1898 there were treated at the United States General Hospital at Fort Myer, Virginia, 719 cases of typhoid fever, which had been sent from the various camps in the South, and the death rate was only 9 per cent. In the Second Division Hospital, at Camp Thomas, the percentage was but little greater, there having been 28 deaths among 278 patients. A report just received by the surgeon-general from the First District United States Army Hospital, at Huntsville, Ala., shows that there were in all 418 cases of typhoid fever admitted at that hospital, of which the mortality was only 8.1 per cent. On combining the experience of the three hospitals we find a total of 1,415 cases, with a death rate of 8.98 per cent.—a remarkably low mortality, considering the depressed condition of many of the patients on entering the hospital.

TREATMENT.

The treatment of typhoid fever will be considered under the following headings: 1. *Prophylaxis.* 2. *General management.* 3. *Diet.* 4. *Special forms of treatment.* 5. *Treatment of special symptoms and complications.* 6. *Management of convalescence.*

Prophylaxis.

Typhoid fever is most commonly conveyed by drinking-water which has been contaminated by the fæcal discharges of a previous case of the disease. Other agencies in spreading the disease, such as infected milk and food, have been referred to under the head of etiology in the preceding article. In rare instances, also, the specific bacilli may be inhaled with dust and swallowed with the saliva. But by far the most frequent mode in which the infection is carried is by water. Prophylaxis

therefore requires, on the one hand, that the water supply should be pure and the drainage efficient; and, on the other, that the discharges of every case of the disease should be at once disinfected and thus rendered harmless. Munich furnishes a striking instance of what can be accomplished by the introduction of an improved system of drainage. Child's figures, quoted by Osler, show that from 1851 to 1860 the mean annual death rate from typhoid fever per 100,000 inhabitants was 202.4; from 1860 to 1896 the mortality has steadily decreased, until in the latter year it was only 5.6 per cent.

General measures of sanitation belong to the domain of public hygiene, but much also remains to be done by the private practitioner. Each individual case of typhoid fever should be considered as a focus of infection, and should be handled accordingly. The proper measures to be taken will be considered presently. A careful search for the source of the contagion should also be made in every case. Should there be the least doubt as to the purity of the drinking-water, it should be boiled before it is drunk, unless a supply from another source can be obtained. If the milk be suspected, the same precaution must be taken with regard to it. In the presence of an epidemic all drinking-water and milk should be thoroughly boiled before they are used. Flies are now known to be sometimes the carriers of typhoid infection. It is probable that they were among the chief agencies in spreading the disease in our home camps during the late war with Spain. All food, therefore, which has been exposed to infection in this manner should be well cooked before it is eaten.

The chief duty, however, of the practising physician lies in preventing the spread of the disease from the patient under his immediate charge. The infection, as already stated, is commonly conveyed in the stools and urine. If there is vomiting it may also be carried in the vomited matters. The bacilli have even been found in the sweat and in the sputum. It follows, therefore, that all the discharges and secretions of the patient should be rigidly disinfected. The stools and urine, however, are the usual media of contagion.

The following measures should be carried out in every case of typhoid fever, whether in private or hospital practice:

1. The stools and urine should be disinfected with lime; either the milk of lime or the solution of the chloride (bleaching powder) may be used. The milk of lime is prepared by carefully adding to fresh unslacked lime, placed in an earthen or wooden vessel, as much water as it will absorb. The slacked lime is then stirred with four parts of water to form milk of lime. The solution of the chloride of lime is prepared by adding six ounces of the powder (containing at least twenty-five per cent. of available chlorine) to one gallon of

water. The chloride of lime should come from a trustworthy source, should be preserved in hermetically sealed packets, and its solution should be freshly prepared. Corrosive sublimate (1:500 acidulated solution) and carbolic acid (1:20 solution) are frequently used in place of the preparations of lime, but are not so efficient. Corrosive sublimate requires contact for at least six hours, and carbolic acid for twenty-four hours for thorough disinfection, whereas lime is effective in one hour. Lime is at once the most inexpensive, the most rapid, and the most practicable disinfectant for fæces.

Formaldehyde, a product of wood alcohol, has recently been strongly recommended for the disinfection of typhoid stools. An eight-per-cent. solution of the gas is employed. It is more quickly effective than lime, but is somewhat more expensive.

2. A half-pint of the disinfectant solution should be placed in the bedpan before it is used, and enough of the solution added to completely cover the stool. The disinfectant and the stood should be thoroughly mixed and allowed to stand in the vessel at least one hour before being thrown into the watercloset. All solid masses of fæces must be broken up with a stick or preferably a glass rod. The stick should be at once burned and the glass rod sterilized. The bedpan must be promptly cleaned with boiling water and the disinfectant solution. Vomited matters and sputa should be disinfected in a similar manner.

3. After each movement the buttocks and anus of the patient should be cleaned with a 1:60 carbolic-acid solution, or a 1:2,000 corrosive-sublimate solution, followed by hot water and soap.

4. The mattress should be protected by a rubber cover placed under the sheet. All body linen and bed clothing used by the patient should be soaked for several hours in a 1:20 carbolic-acid solution, and then boiled for at least a half-hour.

5. Thermometers, rectal tubes and syringes, and all utensils coming in contact with the patient should be cleaned with soap and water, and disinfected with a 1:40 carbolic-acid solution or a 1:1,000 corrosive-sublimate solution.

6. Nurses should wash their hands thoroughly with hot water and soap, and disinfect them with a 1:1,000 corrosive-sublimate solution. This should always be done after handling the bedpan, or using the rectal thermometer or syringe, or after bathing the patient. It is especially important that nurses should observe this precaution before eating.

7. The stools, even after thorough disinfection, should never be thrown upon the ground. In camps or in country districts, where there are no waterclosets or privies, the stools should be mixed with

sawdust and burned, or buried in trenches four feet deep and covered with milk of lime. The trenches should always be distant from any source of water supply, and also far removed from the kitchen or other places where food is kept.

8. Typhoid stools, whether in bedpan or trench, should never be left exposed to the air, but should always be promptly covered with a disinfecting solution.

9. Disinfection of the stools should be continued until the patient is convalescent and is able to leave his bed. The urine should be disinfected throughout convalescence and so long as the patient remains under observation and control.

10. After the death or recovery of the patient the mattress, bedspread, and blankets should be thoroughly aired. If they have been soiled by dejecta, they should be disinfected by steam heat or burned. The bedstead should be washed with hot water and soap, followed by a 1:1,000 sublimate solution. The rubber cover should be well washed with cold water, and, if soiled, had best be burned.

General Management.

There is no disease in which good nursing and careful hygienic management are more important than in typhoid fever. The patient should be put to bed on the first day that the disease is suspected, and he should be kept in bed until thoroughly convalescent. Should he be taken ill at a long distance from his home, he should not be allowed to make the journey there, unless it is absolutely necessary in order to secure proper treatment. All experience shows that those cases do best that have had absolute rest in bed from the beginning of the attack. The low mortality among patients in private practice as compared with those seen in hospital service is largely due to the fact that the former usually come under observation at an early period of the disease. The patient should not be allowed to leave his bed for any purpose whatever until convalescence is well established. The use of the bedpan and urinal must be insisted upon from the beginning. Most patients have difficulty at first in emptying the bowels or bladder in the recumbent position, but as a rule they soon acquire the habit, particularly if the bowels are not allowed to become constipated. Pepper, however, has met with cases in which the effort was without result, and caused such excitement and annoyance that it was necessary to have the patient lifted upon the commode at the side of the bed. In his experience this necessity arose most frequently with young women, but by the use of proper care no ill effects followed in any case.

An intelligent nurse is essential to the proper care of a case of typhoid fever. At the beginning of the illness the attending physician should give to the nurse specific instructions as to the general management of the case, the diet, and the disinfection of the discharges and bed-linen, and should see that his instructions are understood and carried out. At his daily visit he should write out his directions for the twenty-four hours, and should receive from the nurse a written report of the amount of nourishment, number of discharges, and all other clinical data of importance. Constant watchfulness must be maintained from the beginning of the disease to the end of convalescence.

The sick-room should be large and well ventilated, and, if possible, it should have a sunny exposure. It is very desirable to have a second room available, communicating with the first, so that the patient may be transferred from one to the other from time to time. If two rooms are used, the window of the unoccupied room should be kept constantly open day and night. An open fire is much to be preferred to steam or furnace heat. The room should not be too warm. The temperature should be maintained at about 68° F. during the day, with a somewhat lower range at night. Screens are useful, both to guard against direct draughts of air and to soften the light in the room when the patient wishes to sleep.

The bed should be single, so that the patient may be easily approached from both sides by the nurse. The mattress should be neither too hard nor too soft. A feather mattress is very objectionable and should never be used. A woven-wire spring mattress, covered with one of hair, upon which is placed a double blanket, furnishes the best bed for a prolonged illness. A rubber cloth should be spread under the sheet. The sheet should be kept smooth, to prevent the formation of bedsores. The position of the patient should be changed from time to time, so that he may not lie continuously upon any one part of the body. The change of position will aid not only in preventing bedsores, but in lessening the danger of hypostatic congestion of the lungs. The back, the region of the sacrum and the trochanters, and the heels should be bathed at least once a day with alcohol or spirit of camphor. Major William B. Davis, of the United States army, advises that the prominent parts of the back be rubbed with a lemon cut in half. Should a sore appear, it must be treated on antiseptic principles and the parts protected from pressure by a rubber ring or air-cushion. In protracted cases, especially if there is much emaciation, a water-bed may be used with advantage.

The mouth of the patient should receive attention from the beginning. The mouth and tongue should be frequently cleansed with a

soft cloth wet with a solution of borax or boric acid in glycerin and water. The teeth should be kept clean, and the lips moistened if they show a tendency to become dry and cracked. These measures not only contribute greatly to the comfort of the patient, but they tend to prevent the stomatitis which so often leads to inflammation of the parotid or to middle-ear disease.

The patient should receive no visitors. One member of the immediate family may be allowed to be with him, provided no harm seems to result. No unnecessary conversation should be permitted in the sick-room, nor should the patient be informed of any news that would be likely to excite him. Repose of mind is only second in importance to repose of body.

Diet.

The diet should be carefully regulated. All food must be administered in fluid form from the beginning of the disease until the temperature has been normal at least a week. Nourishment should be given frequently and at fixed intervals—at least as often as once in three hours. Milk in some form is by common consent the best food in typhoid fever. It should not be given pure, but always diluted with lime-water or vichy or other carbonated water, in the proportion of one part of the diluent to three or four of the milk. About forty-eight ounces may be given in the twenty-four hours—this amount, if digested and assimilated, will supply sufficient nourishment to the patient in the great majority of cases. Milk is usually well borne, but occasionally, especially if not sufficiently diluted, the stomach will not tolerate it when given continuously for a long period. This intolerance is shown by an increase of the gastric symptoms or by the presence of masses of curds in the stools. In such cases the milk may be replaced in whole or in part by the use of soups or animal broths. Peptonizing the milk makes it more easily digested, or it may be given in the form of whey or buttermilk or kumyss. Some patients can digest milk, but grow tired of it. In such cases the addition of coffee or brandy or rum will render it more palatable. In my own experience, particularly in hospital practice, it is seldom that any food but milk is required from the beginning to the end of the disease. There is no reason, however, why the diet should not be varied occasionally by the use of other forms of liquid nourishment. Of late years I have been accustomed in private practice to allow at least once or twice a day from four to six ounces of meat broth, in place of an equivalent amount of milk. Milk, however, in my opinion, should constitute our main dependence in the great majority of cases of typhoid fever.

Meat broths are useful when milk disagrees or becomes distasteful to the patient. They may be prepared from beef, mutton, veal, or chicken. They may contain a little rice or barley, but should be strained before they are taken. The juice expressed from slightly broiled beefsteak is of great value in typhoid fever, and is usually well borne. If diarrhœa exists, beef and mutton broths are apt to aggravate it and must not be given too frequently. Bouillon or consommé, given either hot or cold in the form of jelly, will be taken by most patients at least once a day for weeks. All the above meat preparations may be rendered more palatable by the addition of fresh vegetable juices. Clam soup and oyster stew are very nourishing, and give agreeable variety to the diet. A raw egg beaten up in a glass of milk, with or without whiskey, may be given with advantage at least once in the twenty-four hours. Wilson is in the habit of giving three or four raw eggs a day, prepared in this manner, to patients requiring strong nourishment. If the yolk of the egg disagrees, the white may be given alone in the form of albumen water. This is prepared by straining the white of the egg through a cloth and mixing it with an equal volume of water, and flavoring it with lemon or with some form of stimulant, such as brandy or sherry. Thin gruels, well strained, made from barley or arrowroot, are sometimes of great service. Farinaceous gruels are especially indicated, according to Gilman Thompson, in cases characterized by rapid and extreme emaciation. As farinaceous substances have a tendency to cause flatulence in typhoid fever, their effect must be carefully watched.

In mild cases with but little impairment of the digestive functions, food may be given every three hours during the day and at intervals of four hours at night. In severe cases, in which only small quantities are borne by the stomach, the intervals of feeding must be shortened to two hours day and night. If the prostration is extreme, it may be necessary to administer nourishment as often as once an hour. It is always desirable to make a distinction between day and night when possible, and it is often a question whether it is better to arouse the patient for nourishment at night or to let him sleep. If he has been suffering from insomnia and has perhaps just fallen into a refreshing sleep, he should not be disturbed for either food or medicine. As a rule, no harm will be done by delaying the giving of nourishment for an hour or two or until the patient wakes. If, on the other hand, there is constant drowsiness day and night, the patient probably needs the food and should be aroused and fed regularly throughout the twenty-four hours. As Pepper has said, the tact and skill of a nurse are in nothing better shown than in dealing with the sleep and the nourishment of fever patients.

Water.—Water should be given freely whether the patient has thirst or not. Water not only quenches the thirst and improves the nutrition of the patient, but it helps in the elimination of waste products through the kidneys and counteracts the tendency to constipation which is so often observed in typhoid fever. In order to insure a sufficient amount, it should be administered at stated intervals, in the same manner as the food. I am in the habit of ordering two quarts of pure water a day, eight ounces being given every three hours in the twenty-four. If eight ounces seems too large a quantity to be taken at one time, the amount should be reduced to six ounces, given at two-hour intervals during the day and every three hours at night. Gilman Thompson very properly advises that the water should not be drunk too soon after the fluid food, but in the intervals, so as not to dilute the gastric juice too much. The systematic administration of water in typhoid fever has grown in favor in recent years, and forms an important part of certain special plans of treatment to be described later.

In addition to water, lemonade or weak cold tea may occasionally be given. The juice of a sweet orange is usually permissible, also coffee or cocoa well diluted with milk, and given in moderate quantities once a day. Effervescent waters are very grateful to the patient, but must be used with caution, because of their tendency to increase flatulence.

Alcohol.—Alcohol should not be given as a matter of routine. It is seldom required during the first two weeks of the disease, and in mild cases it may not be needed at any time. The chief indications for the administration of stimulants in typhoid fever are to be found in the state of the heart, the pulse, the tongue, and the nervous system. If the impulse of the heart grows weak and the first sound obscure, or the pulse becomes soft and compressible or unduly rapid or weak and irregular, alcohol is called for. A dry, brown tongue indicates, as a rule, the need of stimulants, and under their use it will often become moist and clean at the edges. The presence of extreme restlessness or low muttering delirium is usually an indication for the employment of alcohol. Sometimes this condition develops or becomes more marked while the patient is under free stimulation, and the doubt arises as to the possible agency of alcohol in causing it. In such cases it is advisable to diminish the amount of stimulants for twenty-four hours and note the effect. The presence of complications, such as severe hemorrhage, pneumonia, or perforation, is always an indication for the administration of alcohol. The development of the typhoid state, with stupor, low delirium, subsultus tendinum, involuntary evacuations, etc., calls for increased stimulation.

Alcohol is rarely needed in early childhood. Young adults also, of robust physique and temperate habits, do best as a rule without stimulants. Patients beyond forty years of age, on the other hand, are usually benefited by the administration of alcohol in moderate quantity rather early in the disease. Persons who have been intemperate require stimulation earlier and in larger amount than those of abstemious habits. The administration of alcohol in typhoid fever should be carefully watched in each individual case and its effects noted from day to day. In cases of failing circulation it is well to remember that there are other valuable cardiac stimulants. Gilman Thompson reminds us that by giving small doses of digitalis or strophanthus or caffeine, and other remedies in combination with alcohol, much less of the latter will be required, and there is less danger of inducing the alcohol habit. I have found strychnine a most efficient cardiac tonic, given in full doses (one-fortieth grain every four hours) in conjunction with alcohol. As the symptoms improve for which the alcohol is given, the quantity should be steadily reduced. By observing this precaution we may often stop entirely the use of stimulants before the patient passes from under our control, and thus save him from contracting the alcohol habit.

Whiskey is the usual form of alcoholic stimulant employed in typhoid fever, both in private and hospital practice. Brandy is equally serviceable, but is much more expensive. Whichever form of spirit is used, it must be diluted with water or milk. The amount of whiskey required varies of course with the conditions of each case. Two to four ounces a day in divided doses frequently repeated through the twenty-four hours is usually sufficient for cases of moderate severity. In very severe cases, characterized by great prostration, it may be necessary to give as much as eight ounces daily, but it is rarely necessary to exceed this amount. Occasionally twelve ounces a day may be required for a few days to tide over the onset of a complication. The following admirable rules are suggested by Moore, of Dublin, as guides in the administration of alcohol in fever:

"Alcoholic stimulants are doing a fever patient good if, under their use:

"1. The heart's action becomes stronger and less rapid, the impulse increasing in strength, and the first sound becoming more distinct;

"2. A soft, compressible, undulating, irregular, or intermitting pulse becomes fuller and stronger, and more regular in rhythm and volume;

"3. A dry, brown tongue becomes clean and moist at the edges;

"4. Delirium lessens, the patient becoming more tranquil, or even falling asleep."

Some patients, particularly women, do not like whiskey or brandy. In such cases an equivalent amount of port or sherry or other strong wine may be used. If there is vomiting, dry champagne in doses of an ounce or two is recommended by Thompson. Champagne is also serviceable in cases of impending collapse. Strümpell does not hesitate to give beer in moderate amount, if the patient desires it. It is, however, apt to increase gastric catarrh and is not much used in this country. The use of stimulants in convalescence will be referred to later.

Special Forms of Treatment.

Hydrotherapy.

The external use of cold water is the most generally accepted method of treatment of typhoid fever at the present day. It was first proposed in 1786 by James Currie, of Liverpool, who practised it systematically in all forms of continued fever. Some ten years later he published his "Medical Reports on the Effects of Water, Cold and Warm, as a Remedy in Fever and Other Diseases." In this work he described with admirable clearness the class of cases in which he believed the cold-water treatment to be indicated, and laid down strict rules for its administration. Currie employed, as a rule, cold affusions, using salt water of 45° to 60° F., the temperature varying with the season of the year. When cold water could not be obtained, as in the tropics, he advised the use of cool baths (77° to 78° F.), the duration of the immersion depending "on the effects on the pulse, on the sensations, and on the heat, measured by the thermometer." He preferred salt water to fresh, on account of the stimulating effect of sea salt on the vessels of the skin, by which, in his opinion, the debilitating action of cold is prevented. Salt water also, whether for the purpose of immersion or affusion, he found more grateful to the patient than fresh water. Sea water was used when at hand; otherwise a saturated solution of sea salt in water. The effects of the cold affusions, as observed by Currie, were an abatement of the fever, a reduction of the frequency of the pulse with an increase in its force, and a disposition to quiet sleep. Currie's book passed through several editions in the course of a few years, and his methods were followed for a time by many physicians both in Europe and in America. Unfortunately his followers failed to observe the rules and precautions insisted upon by Currie, and the cold-water treatment gradually

fell into disuse. In 1861 it was again brought forcibly to public attention by Ernst Brand, of Stettin, and his vigorous and persistent advocacy of its merits has led to its being called by his name. The Brand method of treatment of typhoid fever is now employed throughout the world. It was slow in obtaining recognition in England, and it is only within the past ten years that it has come into general use in this country.

Hydrotherapy may be applied in various ways, the most important of which are by tub baths, bed baths, the cold pack, and cold sponging.

Tub Baths.—The Brand method of treatment consists in the systematic administration of cold baths, with friction of the body, whenever the temperaure of the patient reaches a certain elevation. Every three hours, if the thermometer placed in the rectum registers 102.5° F., a large bathtub, half-full of water at 70° F., is wheeled to the bedside. The clothes of the patient are removed and he is carefully lifted into the water, which should completely cover his body up to the neck. The head should rest upon a rubber air cushion or other support. The bath lasts fifteen minutes, and throughout the whole period of immersion the body and limbs of the patient should be rubbed vigorously by the attendants, and cold water should be poured upon his head at intervals. The patient should be encouraged to rub his chest and abdomen himself. After the bath the patient is placed in bed and covered with a dry sheet and a light blanket. In some cases the skin is dried at once; in others the patient is allowed to lie for twenty minutes without drying the skin. He is then rubbed dry and reclothed, and his temperature taken to determine the effect of the bath. It is customary to give a half-ounce of whiskey or other stimulant when the patient is removed from the bath. Sometimes it is advisable to give a little stimulant also before the bath. The patient usually begins to shiver when he has been in the water about ten minutes, and the shivering often continues for fifteen or twenty minutes after he has been placed in bed. There is generally also more or less cyanosis, and if this becomes excessive it may be necessary to remove the patient from the bath at the end of ten minutes, rub him dry, and apply hot-water bottles to the legs and feet after he is placed in bed. In other cases, in robust patients with vigorous circulation, the bath may be prolonged to twenty minutes with advantage. The patient usually falls asleep after the bath, and it is not advisable to disturb him. At the end of three hours, however, the temperature should be taken in the rectum, and if it has reached 102.5° F. the bath is repeated. Not more than eight baths should be given in the twenty-four hours.

In beginning the bath treatment, it is sometimes advisable to give the first bath at a temperature of 80° or 85° F., the second at a somewhat lower temperature, and so on until on the third or fourth bath 70° F. is reached. The patient is thus gradually accustomed to the idea of the baths, and often does not notice their increasing coldness. In the treatment of children and old persons, and in cases of great prostration coming under observation late in the disease, the graduated bath of Ziemssen is useful. In this bath the temperature of the water is 90° F. when the patient is placed in it; this is gradually reduced to 72° F. by the addition of ice. The results of the Ziemssen bath are not so good as those of the Brand bath, but it has the advantage that the shock to the patient is not so great. Whatever system of bathing is employed, the physician should always be present at the first one or two baths, in order to note the effects upon the patient and to see that the technique is properly understood and carried out. The only contraindications to the cold-bath treatment, according to Osler, are peritonitis and hemorrhage.

The good effects of the Brand bath, when given systematically as above described, are: 1. The reduction of the temperature; 2. The strengthening of the heart and pulse; 3. The deepening and slowing of the respiration, with diminution of the bronchitis and pulmonary congestion; 4. The improvement of the nervous symptoms; delirium and stupor lessen or disappear, and insomnia is relieved; 5. A marked reduction in the mortality as compared with that under previous methods of treatment. The reduction of temperature effected by the baths varies greatly with the stage of the disease and in different cases. During the first week or ten days there may be a fall of only a fraction of a degree. In some cases during a period of two or three days there may be no change whatever after the bath, and occasionally I have seen the thermometer register one or two-tenths of a degree higher after the bath than before. Sooner or later, however, the most obstinate fever yields, and towards the end of the second week and in the third week the temperature will generally fall from two to five degrees after each bath (see Chart No. 10). In the course of the two or three hours following the bath the temperature usually rises again to about its former level, but, as observed by Baruch, from day to day there will be a gradual yet steady diminution of the average temperature, which indicates that the resisting power of the system is gaining sway over the disease. Chart No. 10 shows the increasing effect of the baths upon the fever with the steady reduction of the average temperature. The effect of the bath upon the circulation is immediate and marked. The heart's action becomes stronger, the pulse slower and fuller. It is not unusual to

see a fall in the pulse rate of from ten to twenty or more beats in the minute. The digestive system is always favorably affected by the cold-water treatment. The tongue becomes moist and clean, and the appetite and digestion improve. The so-called typhoid state is now

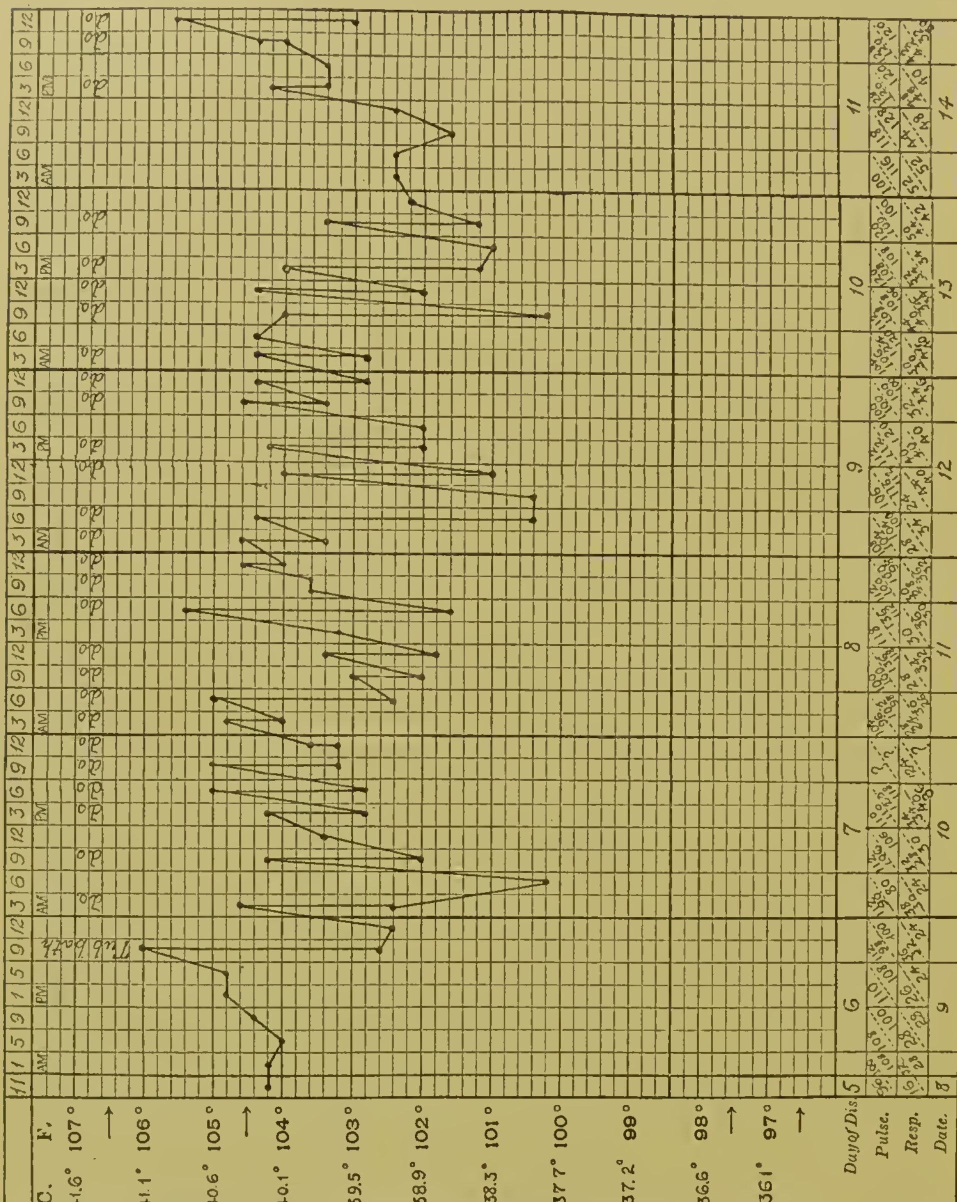

CHART No. 10.—Showing the Effect of Cold Baths in Reducing the Temperature and Lowering the Pulse Rate in a Severe Case of Typhoid Fever.

seldom seen in hospitals in which the baths are systematically administered from the beginning of the disease. The remarkable effect upon the nervous system has already been mentioned, and the most striking evidence of the benefit derived from the baths is afforded by the manner in which a restless, wakeful patient falls into a quiet, refreshing sleep soon after each bath.

The reduction in the mortality of the disease is the most important gain from the cold-water treatment. Previous to the introduction of hydrotherapy, the death rate in hospitals ranged from 17 to

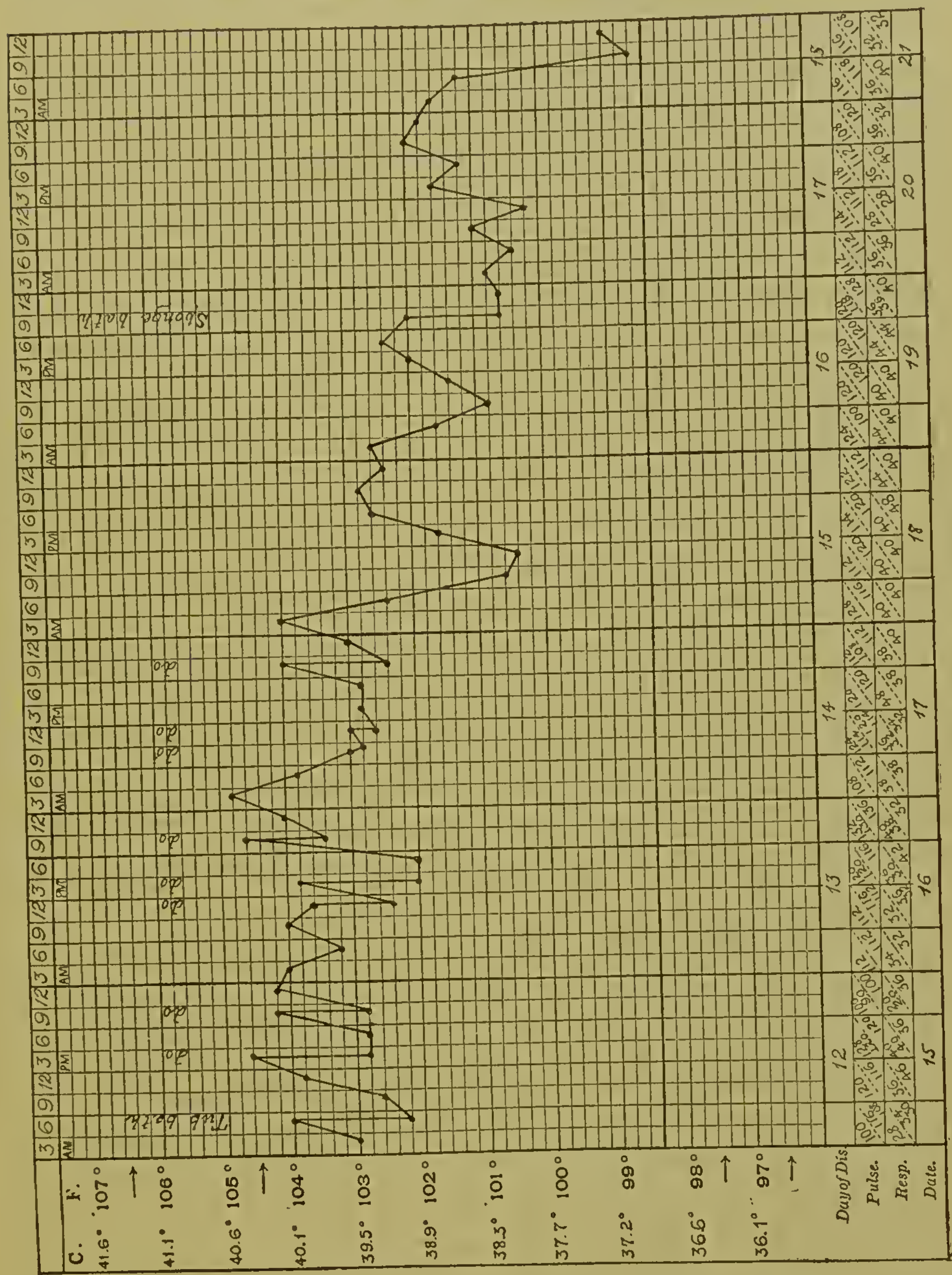

CHART No. 10.—Continued.

25 per cent. The variation in the rate in different epidemics and in different institutions has already been considered in the section on prognosis. Under the Brand treatment the mortality in hospitals has been reduced to 7.5 per cent. and even less. The results in different hospitals in this country are remarkably uniform. Osler

reports a mortality of 7.1 per cent. in the Johns Hopkins Hospital; James C. Wilson a mortality of 7.25 per cent. in the German Hospital, Philadelphia; Tyson a mortality of 7.3 per cent. at the Hospital of the University of Pennsylvania and at the Philadelphia Hospital; and Thompson a mortality of 7.5 per cent. (excluding moribund cases) in the Presbyterian Hospital, New York. Even in Bellevue Hospital, which receives a very unfavorable class of cases, and in which only those of a severe type are, as a rule, subjected to the bath treatment, the death rate among the cases so treated in my series is but 9 per cent.

F. E. Hare has had similar results at the Brisbane Hospital, Australia, his death rate being 7.5 per cent. under hydrotherapy, the mortality under general or expectant treatment having been 14.8 per cent. It might well be inferred from the uniformity of these figures that they represented the lowest point to which the mortality could be reduced by the Brand treatment. Brand himself, however, in his last collection of cases, reported a mortality of only one per cent. His extraordinary results are probably partly due to the strictness with which he enforces his measures, and partly to the fact that his cases, being for the most part in military hospitals, come under observation much earlier than is the case in the civil hospitals in this country. The deaths under hydrotherapy are due, as a rule, to perforation or hemorrhage of the bowel. Tyson states that in all his fatal cases death resulted from one or the other of these two causes. Hare and Osler also found that under the Brand treatment there was no diminution in the number of deaths from perforation or from hemorrhage, the percentage being the same before and after the introduction of bathing.

Bed Baths.—In private practice, and even in hospitals with a very active service, it is often impossible to give frequent baths because of the lack of skilled assistants. At least two nurses are required to lift a patient into a tub. In such cases the patient may be bathed by constructing a tub in the bed in the following simple manner: The blankets and sheets are removed from the bed, and one end of the rubber cover which is already on the bed under the patient is carried up over the pillow; along the sides and foot of the bed tightly rolled blankets are placed, and over these the sides and lower end of the rubber cover are carried in such a manner that the patient lies in a rubber tub from seven to eight inches deep. The tub is now filled with water of the temperature desired and the patient is bathed exactly as if he were in an ordinary tub. It is usually necessary to add ice from time to time, as the comparatively small amount of water in the bed bath is naturally warmed by the body of the patient

more quickly than in the bathtub. When the bath is over, the water is drawn off by siphoning or by removing one of the blankets at the foot or side of the bed and allowing the water to flow into a pail on the floor. The rubber cover is now dried, a fresh sheet passed under the patient, and a sheet and light blanket placed over him as after the tub bath.

In addition to being relieved from the labor of lifting the patient from bed to tub and from tub to bed, the bed bath is much less fatiguing to the attendants than the tub bath because the patient lies at a more convenient height. I have often seen this form of bath given in the women's wards of Bellevue Hospital and can testify to the comparative ease of its administration. It is quite as effective, also, in my experience, as the full tub bath, both in reducing temperature and in stimulating the patient.

The Cold Pack.—This is given as follows: A large woollen blanket is spread upon the mattress, previously protected by a rubber cover. A large coarse linen sheet, wrung out of water of a temperature of from 60° to 70° F., is spread upon the blanket. The patient, with his head covered with a wet towel, is carefully wrapped in the wet sheet from his shoulders to his feet, and is then snugly enveloped in the blanket, the ends of which must be tucked closely around the neck and around and over the feet. Everything depends, according to Baruch, upon complete exclusion of air from beneath the blanket cover. The duration of the pack will depend upon the object for which it is given. If reduction of temperature is the chief aim, the patient must be removed from the pack as soon as it becomes warm and placed in another about two degrees higher. From this pack he is again removed into another of two degrees higher, and this process is repeated until four or five packs have been given or until the temperature approximates the normal. If the patient has marked nervous symptoms and the bath is given for its calming effect the first pack should be prolonged for an hour or more. A restless patient will often fall asleep in the pack, and Baruch advises that he be allowed to sleep until he awakens, and then rapidly sponged with cold water before he is placed in bed.

The cold pack is useful when the tub bath is contraindicated or when it is opposed by the patient or his friends. The cooling effect of the pack is much less than that of the bath. According to Liebermeister, four consecutive cold packs, of from ten to twenty minutes' duration each, are about equivalent in effect to a cold bath of ten minutes. The cold pack finds its especial indication in cases with moderate temperature (101° to 103° F.), but attended with delirium or insomnia or other pronounced nervous symptoms. The pack is also of great service in the treatment of children, when circumstances

make the bath impracticable. Holt writes that the cold pack is one of the simplest and most efficient means of reducing temperature which can be employed. His method of procedure is as follows: The child should be stripped and laid upon a blanket. The entire trunk should then be enveloped in a small sheet wrung from water at a temperature of 100° F. Upon the outside of this, ice may now be rubbed over the entire trunk, first in front and then behind. By this method there is no shock and no fright, and any ordinary temperature can usually be readily reduced. The rubbing with ice should be repeated in from five to thirty minutes, according to circumstances, after which the child may be rolled in the blanket upon which he is lying without the removal of the wet pack. The head should be sponged with cold water while this is being carried on, and artificial heat, if necessary, should be applied to the feet. The pack is continued from one to twenty-four hours, according to circumstances.

A modification of the cold pack was employed with signal success during the summer of 1898, in the camp at Chickamauga in the treatment of the large number of soldiers ill with typhoid fever. The patient was stripped and laid upon a cot covered with a rubber blanket, and the foot of the cot was lowered some six inches. A sheet was spread over the patient and he was then sprinkled with water from an ordinary watering-pot. The duration of the sprinkling was regulated by the condition of the pulse. The water was used just as it came from the pipes which conveyed it over the ground, a distance of three miles from its source in Chickamauga creek. Its temperature was from 90° to 100° F. There was no ice and there were practically no skilled assistants or nurses. Dr. S. Dana Hubbard, of New York, at that time chief surgeon of the Ninth New York Volunteers, and executive officer of the Second Division Hospital, reports that of the two hundred and seventy-eight typhoid patients under his care twenty-eight died, a mortality of only ten per cent. Considering the adverse conditions, this death rate is remarkably low.

Cold Sponging or Ablution.—Sponging, as ordinarily practised, is not very efficient in reducing high temperature. It is, however, refreshing to the patient, and is of value in allaying nervous symptoms, particularly in children. Holt finds its effect often more satisfactory than an anodyne. The water may be tepid, cold, or ice-cold, according to the height of the fever. Equal parts of alcohol and water, or vinegar and water, equal parts of each, may be employed. The stimulating effect may be increased by using a saturated solution of sea salt or water impregnated with the artificial Nauheim salts. Baruch applies the water by the hand, either bare or covered with a bath

glove, or holding a gauze or linen wash cloth. He avoids the sponge, because it does not produce sufficient friction and thus prevents reaction. The stroking with a wet sponge produces cooling by evaporation, but very little irritation of the nerve terminals, and consequently very little if any effect upon the central nervous system, which should be the chief aim of hydriatic procedures. Baruch bathes the patient by freely throwing water from the hollow of the hand or by saturating a crumpled piece of gauze with the water and gently rubbing successive parts, frequently dipping the cloth and squeezing the water out of it over the parts. The gentle shock of the impact of the water applied by these methods is accompanied and followed by gentle friction. When the ablution is complete, the patient, if sufficiently vigorous, is simply wrapped in a dry sheet and allowed to dry spontaneously. In debilitated subjects it is best to bathe and dry the body limb by limb to avoid chilling the surface.

Medicinal Treatment.

Mild uncomplicated cases of typhoid fever require little if any medication. In severe cases, apart from the complications, the chief indication for treatment is furnished by the height of the temperature and this is best controlled by the hydrotherapeutic measures described above. Before the value of the Brand method had obtained general recognition it was the practice to use certain antipyretic drugs for the purpose of lowering the temperature, and they are still employed by some physicians. The most important of these antipyretics are quinine and the coal-tar derivatives.

Quinine, to be effective in typhoid fever, must be given in large doses, grs. xxx. to xlv. in the twenty-four hours. Liebermeister was accustomed to give this amount in divided doses at short intervals, grs. viiss. every ten minutes until the desired quantity had been taken. He insisted that the whole amount should be taken within the space of an hour. The drug was administered at nightfall in order that the effect of the quinine might coincide with the usual morning remission on the following day. The dose was not repeated, as a rule, in less than forty-eight hours. Liebermeister, although a strong advocate of the cold-water treatment of typhoid, was also firmly convinced of the great value of quinine as an antipyretic in this disease. He found it of especial service in those cases in which the fever failed to yield to the cold baths or in which the baths were contraindicated on account of intestinal hemorrhage, or cardiac weakness, or for any other reason. After an experience with fifteen hundred typhoid-fever patients, to whom he had given quinine in large

doses, he states that in no single instance had he seen any permanent injury follow which could justly be attributed to the action of the quinine. Other clinicians, among them Kaulich and Chapetal of Vienna, Senator of Germany, and Germain Sée and Jaccoud of Paris, have followed Liebermeister's method of using quinine in typhoid fever, but there are few physicians at the present time who would venture to give it in the quantities prescribed by him. It is, however, frequently employed in moderate doses as a general tonic. It is, of course, indicated as an antiperiodic in cases complicated by malaria.

The most important of the coal-tar antipyretics are antipyrin, phenacetin, and acetanilid. Some twelve or fifteen years ago, at the time of their first introduction into practice, they were very extensively used in typhoid fever. There is no question that, if given in sufficient dose, they will, as a rule, reduce the temperature promptly. Their use, however, is not unattended with danger. Numerous instances have occurred in which dangerous and even fatal depression and collapse have followed their administration, even in moderate doses. The employment of these drugs as antipyretics should be limited to acute fevers of a sthenic type; they are not suited for continued administration in an adynamic fever of long duration like typhoid. The occasional use of a small quantity as an adjuvant to the cold bath is permissible, but even in such cases it is well to give a stimulant at the same time to counteract any possible depressing action. Reference has already been made to the effect of the coal-tar derivatives in checking the elimination of toxic substances by the kidneys in typhoid fever. Guaiacol, a derivative of beechwood creosote, causes a prompt fall of temperature when painted on the skin of a febrile patient. This action of guaiacol has led to its employment as an antipyretic in typhoid fever. The fall of temperature is, however, only temporary, and is often accompanied by alarming symptoms of depression. The use of guaiacol is therefore open to the same objections as that of the coal-tar derivatives.

Antiseptic Treatment.

The antiseptic treatment of typhoid fever has for its aim the destruction of the typhoid bacilli and their toxic products in the alimentary canal. This treatment is also designed to arrest fermentation and to check the activity of the ordinary intestinal bacteria which are believed to become virulent in consequence of association with the typhoid bacillus. A large number of antiseptic drugs have been employed for the purpose and many competent clinical observers have

reported benefit from their use in typhoid fever. The duration of the disease is not usually shortened, but its course is rendered milder and its mortality lessened. Few clinicians believe that antiseptic medication is equal in effectiveness to the cold-water treatment as applied by Brand. It is intended rather for use in those cases in which, for one reason or another, the Brand method cannot be carried out.

Among the remedies recommended for their antiseptic effect may be mentioned calomel, naphthalin, beta-naphthol, thymol, carbolic acid and tincture of iodine, chlorine water, and salol. Calomel has been used more largely perhaps than any other drug. It is employed not only because of its antiseptic properties, but also because it is a safe and efficient laxative. Liebermeister was one of the first to advocate its use in typhoid fever. He was accustomed to give it in three or four doses of seven and one-half grains each in the first twenty-four hours of treatment. He claimed that under its use the duration of the disease was materially shortened and its intensity lessened. Many other authorities, notably Bouchard, recommend the use of calomel, either in large initial doses after the method of Liebermeister or in small and repeated doses throughout the disease.

Naphthalin was very extensively tried some ten years ago, both alone and in association with calomel. It was first recommended by Rossbach, who believed that it exerted an abortive effect in early cases. The majority, however, of those who used the remedy failed to see any benefit from its use and found it inferior as an antiseptic to other drugs of this class.

Beta-naphthol is a powerful germicide. It is but slightly soluble in fluids and therefore reaches the intestine undecomposed. It is also non-toxic and is said to be non-irritant in doses which are sufficient to exert an antiseptic and disinfectant effect on the bowel. It is given in wafers, capsules, or tablets in doses of gr. v. to x. three to five times a day. Bouchard combines salicylate of bismuth with it if there is diarrhœa, or salicylate of magnesium if there is constipation. Very favorable results have been reported from the use of beta-naphthol. Abdominal pain and meteorism diminish, the tongue becomes clean and moist, and the passages lose their offensive smell. Convalescence also seems more rapid and with less tendency to secondary complications. Thymol is a very efficient intestinal antiseptic. It may be given in doses of from twenty to forty grains a day. Henry, of Philadelphia, has used it in a large number of cases with results similar to those produced by beta-naphthol.

A mixture of carbolic acid and the tincture of iodine, in the proportion of one part of the former to two of the latter, has been rec-

ommended for its supposed specific effect in typhoid fever, in doses of from one to three drops three to six times a day. Many physicians have used this combination with apparently good results. As it is readily absorbed from the stomach it cannot exert any local action in the intestinal canal. Because of its sedative action on the gastric mucous membrane, D. D. Stewart considers it especially indicated in cases in which nausea and vomiting are present.

Chlorine water was recommended many years ago by Sir Thomas Watson and by Murchison, and in recent years its value in typhoid fever has again been strongly urged by Burney Yeo. Murchison regarded it as the most useful of all the antiseptic remedies in use at that time, but in his experience its beneficial effect was confined to its influence upon the abdominal symptoms. Yeo claims for it a much wider range of action. He prepares a fresh solution of chlorine gas as follows: "Into a twelve-ounce bottle put thirty grains of powdered potassium chlorate, and pour on it forty minims of strong hydrochloric acid. Chlorine gas is at once rapidly liberated. Fit a cork into the mouth of the bottle, and keep it closed until it has become filled with the greenish-yellow gas. Then pour water into the bottle little by little, closing the bottle and well shaking at each addition, until the bottle is filled. To twelve ounces of this solution for an adult I add twenty-four or thirty-six grains of quinine and an ounce of syrup of orange peel, and I give an ounce every two, three, or four hours, according to the severity of the case." Yeo reports remarkable results from this combination of chlorine and quinine. The tongue cleans quickly, and the fœtor of the evacuations usually subsides within twenty-four hours after beginning the treatment. There are also a modification and a sustained depression of the febrile temperature, the average course of the fever is shortened, the physical strength and intellectual clearness of the patient are maintained, with less need for stimulants, there is a greater power of assimilating food and a rapid and complete convalescence. Yeo believes that he obtains not only an intestinal but a general antisepsis by this treatment. Many physicians have employed and still employ chlorine water in typhoid fever, either with or without quinine, in the manner recommended by Yeo. The general verdict is that it exerts a favorable influence upon the course of the disease, though I am not aware that any have found it quite so far-reaching in its effects as Yeo claims it to be.

Salol is a very valuable intestinal antiseptic. Like naphthol, it is insoluble in water. It is a compound of salicylic acid and carbolic acid, and is decomposed by the pancreatic juice into these two substances. It may be given in wafers, capsules, or tablets in doses

of from forty to sixty grains a day. It appears to act upon the alimentary canal like naphthol. The tongue cleans rapidly and the stools lose their offensive odor. Salol is also called a urinary antiseptic, as in its elimination it sterilizes the urine (Hare). Mark Richardson has, however, recently reported that the typhoid bacilli may persist in the urine for considerable periods of time in spite of a daily dose of thirty grains of the drug. In one case a patient received thirty grains of salol a day for thirteen days, with no apparent effect on the bacilli. Urotropin, a non-toxic and non-irritating derivative of formaldehyde, was found by Richardson to be much superior to salol as a urinary antiseptic, and he concludes from his experiments that in the great majority of cases urotropin, given for a week in daily doses of thirty grains, will remove typhoid bacilli permanently from the urine.

The Eliminative and Antiseptic Treatment.

The eliminative and antiseptic treatment of typhoid fever has as its object not only the destruction but also the prompt removal of the bacillus and its toxic products. The destruction is accomplished by some one of the methods of intestinal antisepsis just described. The removal or elimination is effected by securing free and thorough evacuation of the bowels daily by means of purgatives. Large quantities of water are also given at frequent intervals to replace the fluid carried off in the discharges. Purgation is not a new method of treatment in enteric fever. Early in this century Stoll and Delarroque and Andral used purgatives freely throughout the disease, and apparently with beneficial effect upon its course. Nor, as we have seen, is the use of antiseptics altogether a modern procedure in the treatment of typhoid fever. But it is only within quite recent years that the two methods have been combined into a systematic plan of treatment.

Woodbridge of Cleveland and Thistle of Toronto, working independently of each other, are the two chief exponents and advocates of the use of purgatives and antiseptics in typhoid fever. The method of Woodbridge is as follows: On the appearance of the earliest symptoms of fever and without waiting until a positive diagnosis is made, the treatment is begun with tablets each of which contains:

No. 1.

Podophyllin resin,	gr. $\frac{1}{960}$
Calomel,	gr. $\frac{1}{16}$
Guaiacol carbonate,	gr. $\frac{1}{16}$
Menthol,	gr. $\frac{1}{16}$
Eucalyptol,	q. s.

One tablet of this formula is given every fifteen minutes during the first twenty-four hours, and in larger doses if necessary during the second twenty-four hours, until during this and the succeeding twenty-four hours not less than five or six free evacuations of the bowels are secured during each of these periods. On the third or fourth day of treatment the following tablets are used:

No. 2.

Podophyllin resin,	gr. $\frac{1}{200}$
Calomel,	gr. $\frac{1}{16}$
Guaiacol carbonate,	gr. $\frac{1}{4}$
Menthol,	gr. $\frac{1}{16}$
Thymol,	gr. $\frac{1}{16}$
Eucalyptol,	q.s.

One tablet is given every one or two hours. This formula and also formula No. 1 should be given as freely as possible at first, then gradually reducing the size and frequency of the doses, the object being so to regulate them as to allow the movements of the bowels to become less and less frequent until the temperature has dropped to normal, when the movements should have been reduced to one or two each day. About the fourth or fifth day of the treatment the employment of the following capsules is commenced:

No. 3.

Guaiacol carbonate,	gr. iij.
Thymol,	gr. i.
Menthol,	gr. ss.
Eucalyptol,	♏ v.

One capsule to be given every three or four hours alternating with the tablets. During all the course of treatment the patient must wash down each dose of medicine with large draughts of distilled or sterilized water, or, if indicated, some good laxative or diuretic mineral water.

Woodbridge asserts that "death is a wholly unnecessary consequence of typhoid fever, and that every case in which the above treatment is instituted sufficiently early in the course of the disease can be aborted." He claims also that he has "thus far been able to abort the disease in every instance in which treatment was instituted on or before the eighth day, and in a large percentage of those cases in which it was commenced on or before the tenth day of sickness, as well as in a few cases taken at a much later period." He does not consider it necessary to confine the patient to bed, nor to restrict his diet to any great extent. In his recently published book

"Typhoid Fever and its Abortive Treatment," he states that "the patient who has been put under this treatment early in the course of the disease need not go to bed or in any great degree be restricted in diet, debarred from social enjoyment, or even be required to neglect or omit his attendance upon his business." In this book, as well as in his other published writings, a large number of cases are given, accompanied with charts, in which the temperature touched the normal point on the tenth day of treatment and the patient was well and able to attend to his ordinary affairs.

Thistle employs no complicated formulæ, and his whole plan of treatment is exceedingly simple and correspondingly easy to carry out. The purgative medicines chosen are those that act on the upper and smaller intestine. Perhaps the most satisfactory is the combination of calomel and salines. Other purgatives, however, may be given, such as cascara sagrada, Seidlitz powders, Carlsbad salts, or compound cathartic pill. Of the antiseptics his chief experience is with salol and his practice is to give it in five to ten grain doses every three or four hours. Thistle holds that antiseptics may be given in much larger doses and with greater freedom from the occurrence of symptoms due to the antiseptic, if associated with the frequent administration of purgatives. To compensate for the withdrawal of so much fluid from the body by such frequent purgations, as well as to dilute and facilitate the elimination of the typhoid poison through the kidneys, the ingestion of large quantities of water is enjoined. Reduced to its simplest terms the treatment may be outlined as follows: Calomel is given daily in fractional doses, one-half grain every half-hour until three grains have been taken, followed three hours later by Epsom or Rochelle salts in half-ounce doses. Sufficient calomel and salines should be given to secure from three to five movements daily. For intestinal antisepsis salol is given in five-grain doses, with eight ounces of water, every three hours.

Thistle, in one of his recent papers, reports 172 cases treated by himself and other physicians in Toronto according to his method, with 5 deaths, or a mortality of 3 per cent. No cases are excluded, whether coming under treatment early or late. Of the fatal cases, 2 died of pneumonia in early convalescence, 2 of intestinal hemorrhage, and 1 of hemorrhage from the stomach and nose with general purpura and hemorrhage from all parts of the body. The two cases of intestinal hemorrhage came under observation in the third week of active illness. In addition to these two fatal cases, intestinal hemorrhage occurred in six cases that recovered. There was no death from toxæmia, and no instance of perforation. Tympanites never developed in any case while under treatment, and when present at first invariably

disappeared as soon as elimination was freely secured. Delirium was practically unknown after the first days. Out of sixty-four charts in his possession, Thistle continues, fifty-eight show that the highest temperature reached was in the first three days. That is, the temperature inclined towards normal as soon as elimination was secured. Several charts are presented in which the temperature descends as regularly as a flight of steps, reaching normal on from the seventh to the tenth day of treatment. The charts seem like duplicates of those published by Woodbridge. All the other symptoms improved with the decline of the fever.

In order to form some estimate of the value of the eliminative and antiseptic treatment of typhoid fever I have employed it in a considerable number of cases during the past two years. I have also collected all the records that were available of cases treated in hospitals by other physicians. I have succeeded in obtaining the full histories and charts of seventy-eight cases, fifty-two of which were treated strictly according to the method advocated by Woodbridge, the other twenty-six after the plan followed by Thistle. Each group of cases will be considered separately.

Fourteen of the cases in the first group were treated in New York hospitals. Four of these were under the care of Dr. Woodbridge himself, who directed their treatment, in the wards of Dr. Charles L. Dana in Bellevue Hospital. Two cases were treated by Dr. H. P. Loomis in the New York Hospital, one by Dr. Charles W. Nammack in Bellevue Hospital, one by Dr. F. H. Daniels in the Manhattan Hospital, and six by myself in Bellevue Hospital. Thirteen cases recovered and one died, the fatal case being one of Dr. Woodbridge's four cases. Two cases were complicated with pleurisy with effusion, the complication being present when the patients entered the hospital. These two cases were also under Dr. Woodbridge's care. The other cases presented the regular course of uncomplicated typhoid fever of moderate severity. One patient had a relapse beginning on the thirtieth day of the disease. All the cases were treated with the tablets prepared by Parke, Davis & Co. according to Dr. Woodbridge's formulæ. The six cases under my observation all ran a favorable course, but in no instance was the disease aborted, although the treatment was begun in one case as early as the sixth day. Chart No. 11 shows the temperature curve in this case. Although of only moderate severity, with the temperature never above 104°, the normal point* was not reached until the twenty-ninth day of treatment and the thirty-fourth day of the disease. In this case, as in all the others, both the spirit and

* The first day of normal temperature refers to the first day on which the temperature was below 99° throughout the twenty-four hours.

the letter of Dr. Woodbridge's instructions were followed. I was not content with simply giving the required number of tablets, but I saw

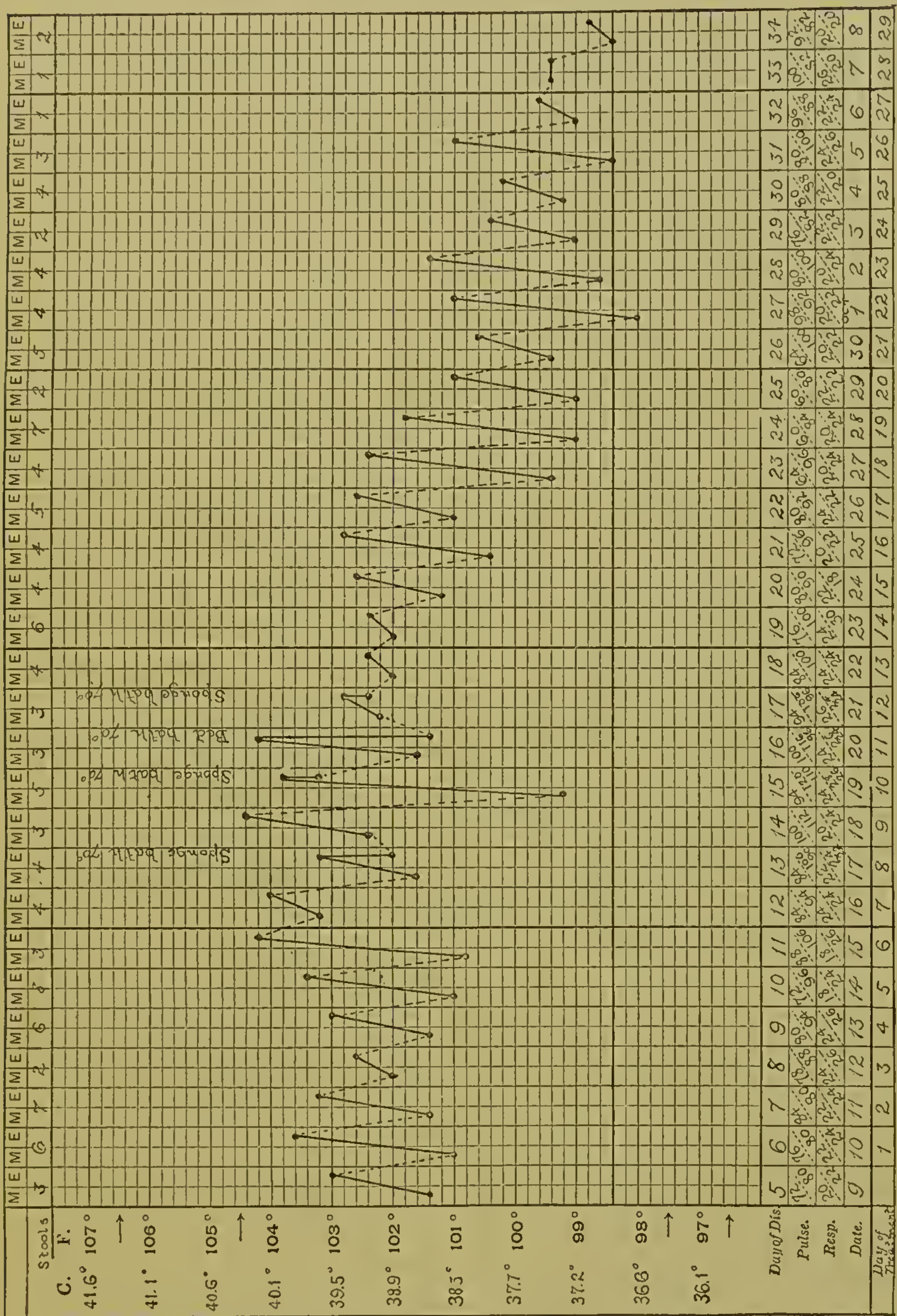

CHART No. 11.—Typhoid Fever Treated by the "Woodbridge Method." Treatment begun on the sixth day of the disease. The night temperatures are indicated by the dotted lines.

to it that the proper number of stools was secured in the twenty-four hours. The chart shows that in this particular case the number ranged from two to eight per day. Of the remaining five cases, one

entered the hospital on the eighth day of the disease, one on the ninth, one on the tenth, one on the twelfth, and one on the fifteenth. Treatment was begun on the following day in every case. The average day on which treatment was begun was the twelfth, and the temperature became normal, on the average, on the twenty-seventh day of the disease, or the sixteenth day of the treatment.

The results in the thirteen cases taken as a whole were not so favorable, probably because some of the cases were more severe than those under my care. Normal temperature was not reached, on the average, until the thirty-second day of the disease, or the twentieth of treatment.

In order to compare these results with those obtained in the same hospital under other methods of treatment I have taken twenty cases which entered Bellevue Hospital during the summer and autumn months of 1896, 1897, and 1898. Nine of the twenty cases were treated with tub baths, and stimulants and tonics as indicated. The others received simply expectant treatment. The twenty cases entered the hospital, on the average, on the eleventh day of the disease. Treatment was begun on the following day, and the temperature became normal on the thirty-second day of the disease and the twenty-first day of treatment.

The remaining thirty-eight cases of this group were treated by Dr. Woodbridge in the United States General Hospital at Fort Myer, Va., during the summer and autumn of 1898. By the kind permission of Surgeon-General Sternberg I have been furnished with copies of the charts and clinical histories of all these cases. Four of the patients died, three of intestinal hemorrhage and one of exhaustion, giving a mortality of 10.5 per cent. for the thirty-eight cases, as compared with a death rate of 9 per cent. among the cases treated in the other wards of the hospital. The four fatal cases came under treatment on the fourth, seventh, eighth, and ninth days of the disease. Thirty-four patients recovered. The average day on which treatment was begun in these cases was the eighth, and the temperature reached normal, on the average, on the twenty-ninth day of the disease, or the twenty-second day of treatment. There were relapses in seven cases of the thirty-eight, a much larger proportion than occurred among the other cases in the hospital. For the purposes of comparison with the cases that recovered, Dr. J. J. Curry, the pathologist of the hospital, has kindly forwarded to me copies of the records of twenty-four unselected cases taken from the other wards of the hospital. These cases were under the general treatment laid down by Major William B. Davis to be followed in all the wards of the hospital, with the exception of the one ward which he had placed

under the charge of Dr. Woodbridge. This treatment is so judicious and well rounded that I shall describe it in brief outline. On entrance, the bowels were thoroughly moved with calomel and soda, then Burney Yeo's chlorine mixture was given, one ounce every three hours, also a glassful of boiled and iced water every four hours. Cold sponging was used when the temperature was between 100° and 102.5°, and iced baths, with friction of the body, when above that figure. Strychnine was administered hypodermically, and whiskey *pro re nata* as soon as the heart showed slight signs of weakness. Unless the patient had one or two movements a day calomel in broken doses was given, followed, if necessary, by Seidlitz powder. The main value of the Yeo chlorine mixture, in Major Davis' opinion, seemed to be that it so modified the typhoid toxin as largely to do away with nervous symptoms. After two weeks' treatment with the chlorine mixture, in each case it was stopped and salol in ten-grain doses *t.i.d.* substituted, as by that time the patient had become much opposed to it on account of the taste. The diet was milk and broths until the temperature had been normal for ten days. This treatment has been employed by Major Davis for many years, and was instituted at the Hospital at Fort Myer one month before Dr. Woodbridge came. On analyzing the records of the twenty-four cases subjected to this treatment it appears that the temperature reached normal, on the average, on the twenty-fourth day of the disease, or the nineteenth day of treatment.

In the following table I have combined in Group A all the cases treated by the Woodbridge method, both in New York and at Fort Myer, and in Group B the forty-four cases treated by the usual methods in Bellevue Hospital and in the United States Hospital at Fort Myer:

TABLE SHOWING COMPARATIVE RESULTS OF THE WOODBRIDGE AND OTHER METHODS OF TREATMENT OF TYPHOID FEVER. (COMBINED EXPERIENCE OF BELLEVUE HOSPITAL AND UNITED STATES GENERAL HOSPITAL AT FORT MYER.)

	Group A. Forty-seven cases treated by the Woodbridge method.	Group B. Forty-four cases under other treatment (baths, etc.).
Day of disease on which patient entered hospital...	8th day.	8th day.
Day of disease on which treatment was begun	9th "	8th "
Day of disease on which temperature reached normal.	29th "	27th "
Day of treatment on which temperature reached normal	21st "	20th "
Number of days in hospital.....	39 days.	40 days.

From this table it appears that the clinical course of the disease was practically the same in the two groups of cases. The patients entered the hospital at the same period of the disease—early in the second week—defervescence took place on very nearly the same day, and the average length of stay in the hospital was about the same. The slight difference of a day or two would probably disappear if the number of cases were larger. In no single instance could it be said that the disease was aborted. We have already stated that there were five deaths in the total number of fifty-two cases treated according to the Woodbridge method, a mortality of 9.6 per cent. We must conclude, therefore, that this method of treatment does not always prevent death nor does it abort the disease, even when instituted early in its course. I shall defer giving my general impressions of the value of the treatment until I have described the results obtained by the Thistle method, for I regard the two plans of treatment as essentially the same.

The second group of twenty-six cases were treated by myself during the autumn months of 1898, with calomel, Epsom salts, and salol according to the method advocated by Thistle. In several of the cases Burney Yeo's chlorine water was used instead of the salol. About one-half of the patients were soldiers who had acquired typhoid fever in the army camps, the others were women and children. Most of the patients were sponged with cold or cool water, some received tub baths when the temperature or other symptoms called for them, all were given stimulants when needed, but not as a matter of routine. One patient, a woman who entered the hospital on the fifteenth day of the disease, died forty days later. During her stay in the hospital she received seventy-seven bed and sponge baths, her temperature ranging above 104° a large part of the time (see Chart No. 3). The remaining patients recovered. There were no complications, but relapses occurred in three cases, or in 11.5 per cent. Treatment was not begun, on the average, until the twelfth day, as the cases came under observation late in the disease. The temperature became normal on the twenty-sixth day of the disease and the fifteenth of treatment. Five of the twenty-five patients were children in whom the fever lasted twenty-one days, on the average, with twelve days of treatment. Excluding these five cases, the duration of the fever for the remaining twenty is lengthened to twenty-eight days, and of treatment to sixteen days. I have placed the adult cases in Goup C, and compared them in the following table with those in groups A and B.

TABLE SHOWING COMPARATIVE RESULTS OF THE WOODBRIDGE, THISTLE, AND OTHER METHODS OF TREATMENT OF TYPHOID FEVER.

	Group A. Forty-seven cases treated by the Woodbridge method.	Group B. Thirty-seven cases under ordinary treatment (baths, etc.).	Group C. Twenty cases under Thistle treatment.
Day of disease on which patient entered hospital....................	8th day.	8th day.	12th day.
Day of disease on which treatment was begun	9th "	8th "	13th "
Day of disease on which temperature became normal....................	29th "	27th "	28th "
Day of treatment on which temperature became normal	21st "	20th "	16th "
Number of days in hospital.........	39 days.	40 days.	39 days.

Personal Impressions of the Eliminative and Antiseptic Treatment of Typhoid Fever.—The above report and analysis of cases show, as I have already stated, that this method of treatment does not abort the disease nor does it always prevent death. On the other hand, the rate of mortality is not high, there being but six deaths in the total number of seventy-eight cases, or 7.7 per cent. The results, therefore, so far as the mortality is concerned, compare very well with those obtained by the cold-bath treatment. There was also a noteworthy absence of complications. Excluding the two cases in which pleurisy with effusion was present when the patients entered the hospital, not a single complication occurred among the seventy-eight cases. The absence of intestinal hemorrhage in the seventy-two patients who recovered testifies strongly to the harmlessness of active purgation in typhoid fever, especially when we consider the advanced stage of the disease at which many of the cases come under treatment. In several other respects I have been favorably impressed by the treatment. In a number of the cases under my care delirium and somnolence were marked at the time of entrance into the hospital, but in every instance these symptoms subsided in a few days, quite as promptly, in fact, as under the use of cold baths. Tympanites also disappeared very rapidly, never calling for any especial treatment. The patients, in a word, did well, much better than under simple expectant treatment and fully as well as under the Brand method, as I have seen it applied in the hospitals of this country. The principles underlying the eliminative and antiseptic treatment seem to me to be sound, even though the results fall short of the claims of its chief advocates. I can see no advantage in the use of the rather fantastic formulæ devised by Woodbridge, and the constant dosing of the patient throughout the twenty-four hours causes needless annoyance

to both patient and attendants. The simpler method of Thistle answers every purpose, and is easily carried out by a nurse of average intelligence.

Specific Treatment with Bacterial Cultures or Serum.

The term "specific" was formerly applied to the treatment of typhoid fever by carbolic acid and other agents, which, by virtue of their antiseptic power, were believed to exert a specific or antidotal action on the disease. The term is now applied to the method of treatment by inoculation of attenuated bacterial cultures, or of antitoxic or bactericidal serum derived from them. The employment of bacterial products in typhoid is somewhat analogous to the treatment of tuberculosis with tuberculin, while the use of antitoxic or bactericidal serum is based on the same principles as its use in diphtheria. The actual value of this method of treatment of typhoid fever is as yet undetermined, but the results so far obtained are interesting and deserve careful consideration.

Treatment by Attenuated Bacterial Cultures.—E. Fraenkel, in a paper entitled "The Specific Treatment of Typhoid Fever," described in 1893 a method of treatment by deep subcutaneous injections of sterilized cultures of typhoid bacilli grown in thymus bouillon. The injections were given in initial doses of .5 gm. of the culture deep into the gluteal region, followed on the next day by 1 gm. The second injection was usually attended by a slight rise of temperature, sometimes accompanied with a chill. The injections were now continued in increasing amounts at forty-eight-hour intervals until from 4 to 5 gm. were given at a dose. On the sixth or eighth day of treatment the temperature usually fell to normal. At the same time the pulse diminished in frequency, the nervous symptoms disappeared, the tongue became clean, and the patient entered upon convalescence. Even in those cases in which the fall of temperature was not complete the fever changed from the continuous to the remittent type, and the duration of the disease was shortened. Fraenkel treated fifty-seven cases in all, and in the great majority the treatment was effective. Neither complications nor relapses were prevented, but the latter yielded promptly to further injections of the thymus culture.

Th. Rumpf repeated the experiments of Fraenkel, but employed cultures of the bacillus pyocyaneus in place of the typhoid bacillus. His results were similar to those of Fraenkel's, but not quite so favorable. He treated thirty patients, two of whom died, one of pneumonia and one of intestinal hemorrhage. Several other observers have made trial of this method of treatment of typhoid fever.

Von Jaksch treated nine cases with cultures of the typhoid bacillus and eight with cultures of the bacillus pyocyaneus. He was not favorably impressed with the treatment, although in both series of cases the continuous was changed to a remittent fever, and the duration of the disease was shortened. These results, however, were not obtained in severe cases. The injections, also, were unpleasant and painful to the patients. In one case which came to autopsy, sterile pyocyaneus pus was found in the injection wound. Kraus and Buswell tried the pyocyaneus thymus culture in twelve cases, of which ten recovered and two died. The injections were made into the thigh and were followed by a limited lymphangitis and abscesses in two cases. Only three cases showed positive results on the temperature. One case showed marked general improvement, though there was no decided fall of temperature. These observers concluded that the treatment had no specific curative value.

The only observations on this method of treatment recorded in this country are those of A. Lambert, of New York, and G. B. Henshaw, of Boston. Lambert reported in April, 1895, the results obtained in twenty-eight cases treated in the hospital service of various New York physicians with a typhoid thymus bouillon prepared by himself according to the method employed by Fraenkel. Of the twenty-eight cases fifteen showed more or less improvement, which could, he thought, be fairly attributed to the injections. Twelve did not improve under the treatment, and one death occurred. In the fifteen cases showing improvement the injections were begun usually about the tenth day, ranging from the sixth to the fifteenth. In the twelve cases showing no benefit from the treatment, the injections were begun at a time varying from the ninth to the twenty-second day of the disease, averaging on the fifteenth day. This is five days later than in the group of improved cases, and bears out the statement of Rumpf that the earlier in the disease the injections are begun the more chance there is of a beneficial action. In the first two cases treated, the injections were given in increasing amounts at forty-eight-hour intervals, as advised by Fraenkel. Later it was deemed expedient to shorten the interval, and the injections were given every twenty-four hours. This gave much better results, both in regard to the temperature curve and in the general improvement of the patient.

Ten of the twenty-eight cases reported by Lambert were treated by myself, either in my wards at Bellevue Hospital or in the service of Dr. William H. Draper at Roosevelt Hospital. In five of the ten cases the results of the injections were well marked. The effect was so striking in one instance that I shall give a brief account of the case. The treatment was begun on the eighth day of the disease—as

soon as a positive diagnosis had been made. Half a gram of the typhoid bouillon was given on the first day, the next day 1 gm., the third day 2 gm., the fourth day 4 gm., and the fifth day 5 gm. The temperature was not affected by the injections until the fifth day, when it fell rapidly and reached the normal in thirty-six hours and remained there. All other symptoms improved at the same time in the manner described by Fraenkel. The patient, who during the treatment had complained bitterly of the soreness caused by the injections, was very grateful for the relief produced by them. Some ten days later a relapse took place, and the patient begged to have the injections repeated. Unfortunately, the supply of thymus solution was exhausted, and the ordinary treatment, including the use of baths, was employed. Under this treatment the relapse, as shown by Chart No. 12, lasted thirteen days—fully twice as long as the primary attack. As relapses in typhoid fever are usually of shorter duration than the original attack, the result in this case seemed to speak for the efficacy of the treatment. I gave all the injections myself—some fifty in number in the ten cases—and I saw no harmful results, either local or general. In two cases, including the one related, temporary soreness was caused by the larger doses, but nothing more.

Henshaw treated thirteen cases with typhoid thymus bouillon, and in his paper gives full histories with charts of all the cases. The results seemed marked in eight cases, in four the course of the fever was not materially affected, and there was one death from intestinal hemorrhage. As it has been suggested that the favorable effect of this treatment is perhaps due to the thymus extract, one case was injected with plain sterilized thymus bouillon, without inoculation of typhoid bacilli. There were no appreciable changes in the temperature chart nor in the condition of the patient at any time. This seems to prove that the presence of the typhoid organisms is essential to the success of the treatment. Henshaw suggests the use of more concentrated and stronger cultures and, if possible, earlier and more persistent injections than were given in the cases so far reported.

Sterilized typhoid cultures have been employed by several experimenters for immunizing purposes. Wright and Semple have prepared a vaccine, using measured quantities of dead typhoid bacilli which had been grown in broth. Eighteen medical officers of the Army or Indian Medical Service were inoculated with the vaccine. Their blood gave the Widal reaction after inoculation, and Wright and Semple believe that they were rendered immune to typhoid fever. Levy, of Heidelberg, and R. Pfeiffer have also used typhoid cultures as a vaccine, with results similar to those obtained by Wright and Semple.

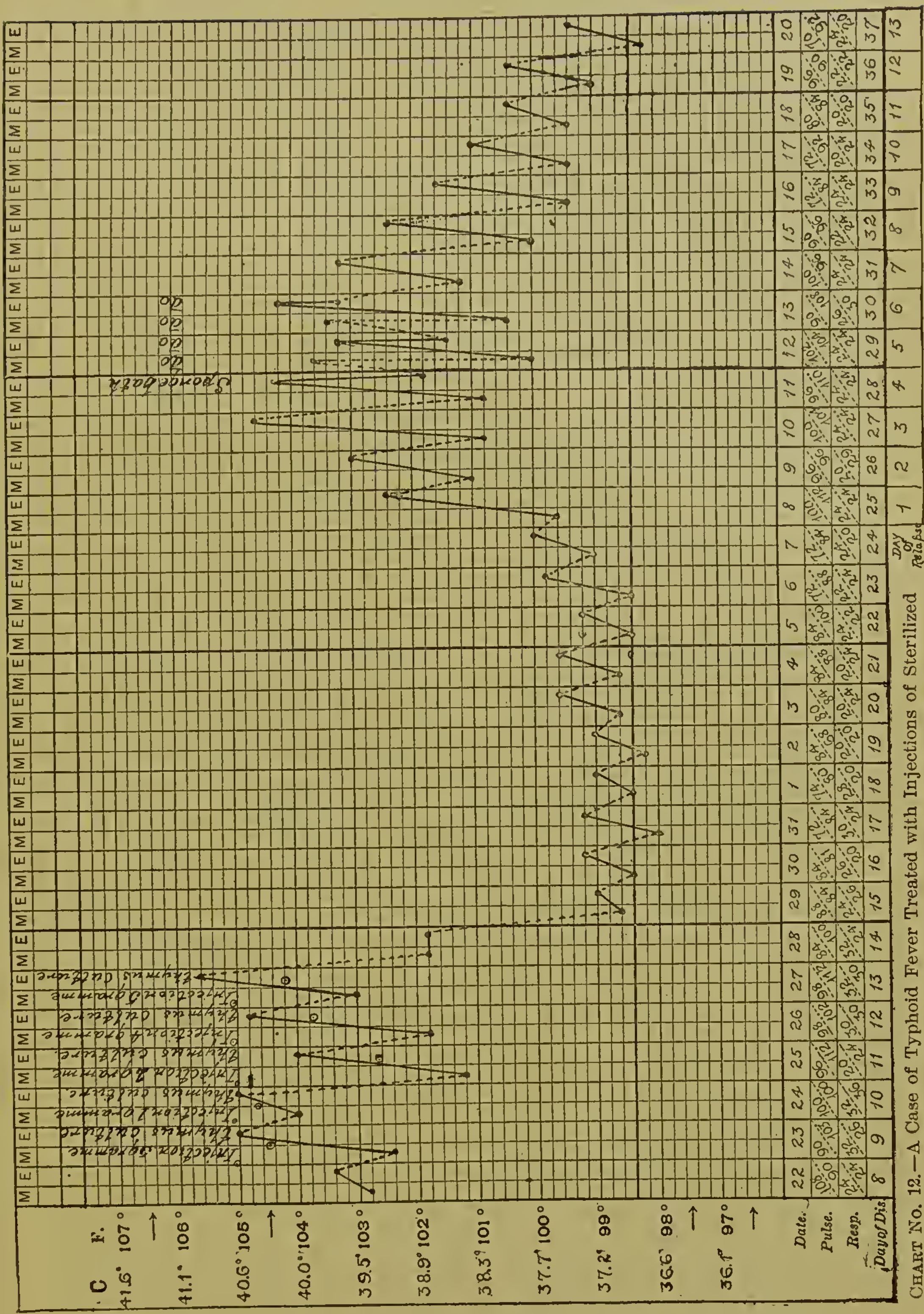

CHART No. 12.—A Case of Typhoid Fever Treated with Injections of Sterilized Cultures of Typhoid Bacilli; the relapse treated by sponge baths.

Treatment by Antityphoid Serum.—Chantemesse, Bokenham, and Hiss have each prepared an antitoxic or bactericidal serum by injecting horses with gradually increasing doses of the typhoid bacillus

and its toxins. Chantemesse has treated a number of cases of typhoid fever with his serum and believes it to have considerable therapeutic value. Under its use the nervous symptoms abate, the temperature is lowered, and recovery hastened. Further experimentation is needed to determine its exact value.

The serum prepared by Bokenham has been used with apparent good effect in a limited number of cases. Pope treated four cases during the height of the fever and noted a steady defervescence from the date of the injections. The temperature came down by lysis, the pulse improved, the tongue cleaned, and the patients looked better. Cooper and Steele observed equally good results in two cases treated by them.

S. W. Lambert treated two cases in the New York Hospital with the serum prepared by Hiss. One patient died, the other recovered. There was no appreciable effect upon the course of the disease in either case. The strength of the serum employed in these cases is such that .05 c.c. will protect a guinea-pig from death if injected into the peritoneal cavity at the same time with double the fatal dose of a bouillon culture of the typhoid bacillus.

Other experimenters have employed the blood serum of patients convalescent from typhoid fever. Silvestri treated two very severe cases which were rapidly growing worse under other treatment, including cold baths. He gave in one case 14 gm., in the other 20 gm., in two doses. Both patients improved in a remarkable manner and convalesced rapidly. The heart's action was strengthened, and the nervous symptoms disappeared. The temperature remained unchanged for four days in one case, but all the other symptoms improved. Jez, on the other hand, reports six cases in which he used serum from convalescents in doses as high as 30 to 35 gm., with absolutely no effect. He believes that the antitoxic and protective bodies in the serum from convalescents are too few to be efficient in typhoid fever in man, although they are effective in small animals, such as mice and guinea-pigs. Pollak's results were but little better in eighteen cases to which he gave injections of serum from convalescents in quantities of from 2 to 45 gm. In three very mild cases the temperature fell after the injections and did not rise again. As a rule, there was a sudden rise of temperature immediately after the injection, but no subsequent improvement. In one case indeed this rise of temperature was followed by collapse. There was no effect on the abdominal or cerebral symptoms. In one case an abscess formed at the site of injection; in six others there was local tenderness. In nearly all the cases decided leucocytosis developed in the course of the treatment.

Treatment of Special Symptoms and Complications.

Headache.—Headache requires, as a rule, but little special treatment. The room should be darkened, and perfect quiet maintained. Cold may be applied to the head, or lotions of menthol or camphor or cologne. Sometimes hot applications are more grateful to the patient. A capsicum plaster to the nape of the neck is often of service. If the headache persists in spite of these measures, it may usually be relieved by small doses (gr. iii.–v.) of phenacetin or antipyrin repeated at short intervals. Pepper advises the use of a suppository of extract of opium, gr. ss., with quinine, gr. v.–viii., when the pain is not allayed by the above remedies. The headache usually disappears spontaneously early in the second week, but I have the notes of one case in which it continued into the fourth week, and was relieved only by twenty-drop doses of laudanum.

Insomnia sometimes calls for active treatment. Bromide of sodium (gr. xv.) and chloral hydrate (gr. viii.) in combination, are probably the most efficient hypnotics we possess for use in the insomnia of typhoid fever, though Dreschfield advises that they should not be given if the heart's action is weak. I have never seen any ill effect from their administration in the above dose. Codeine, gr. $\frac{1}{4}$–$\frac{1}{2}$, acts well in some cases, also sulphonal or trional, in doses of fifteen to thirty grains. An occasional hypodermic injection of morphine (gr. $\frac{1}{8}$) may be given at nightfall, and usually has a most happy effect.

Delirium, somnolence, and restlessness are best relieved by hydrotherapy. These symptoms are rarely prominent in cases which have been treated by cold baths from the outset. If delirium persists in spite of the baths, an ice cap may be placed upon the head and morphine given hypodermically. When the symptoms suggest the onset of meningitis, Tyson recommends leeches to the temples or behind the ears, adding that he has seen an almost magical quieting effect thus produced. Blisters are condemned by both Tyson and Osler. For the nocturnal restlessness, Osler gives Dover's powder. Among the milder remedies, the bromides, camphor, and valerian are all useful. It should not be forgotten that restlessness may be caused by an overdistended bladder. Active delirium is often best controlled by a hypodermic injection of hyoscine (gr. $\frac{1}{200}$) repeated in two hours if necessary. Two or more of these drugs in combination will frequently act better than one of them alone. Sometimes the delirium and restlessness are due to exhaustion, and are then to be treated by increased alcoholic stimulation. Good nursing is indispensable in the management of delirious patients. A soothing voice

and touch may accomplish more than all the sedatives just enumerated. Above all, we must remember that patients in delirium must never be left alone, as cases have occurred in which, during the momentary absence of the nurse, they have thrown themselves from the window to the street below.

Epistaxis may usually be checked by the use of styptics locally or the application of ice to the forehead or to the back of the neck. If it is profuse and persistent it may be necessary to plug the nostrils. Roche has recently reported that a hot flaxseed poultice applied to the nape of the neck will arrest epistaxis immediately. He says that this has never failed in his experience, and has succeeded in several instances when other measures, such as compression, ice, and astringents had failed to arrest the bleeding. Another recent writer recommends pressure with the thumb and finger of the arteries on either side of the bridge of the nose.

Vomiting is not a common symptom in typhoid fever except at the outset of the disease. If it continue long after the patient comes under treatment it is usually an indication that the food disagrees. In such cases all food and medicine should be temporarily withheld. Milk and lime water, equal parts, given a teaspoonful at a time every half-hour, is usually well borne and supplies some nourishment to the patient. Both Wilson and Pepper advise fractional doses of calomel at short intervals, alone or combined with bismuth. Dilute hydrochloric acid in fifteen-drop doses every three hours is often of service. Bismuth in powder (gr. x.) with cocaine hydrochlorate (gr. $\frac{1}{4}$) is recommended by Dreschfeld. A mustard plaster should be applied to the epigastrium in all cases of persistent vomiting. Iced dry champagne in small amounts may be given. Pepper also advises the use of very hot water in teaspoonful doses, or of small pieces of ice.

Tympanites is frequent in typhoid fever. Turpentine is most frequently employed for its relief, either in the form of stupes to the abdomen, or in emulsion by the mouth, or by rectal injections. It is usual to combine the stupes with one or the other method of internal administration. Osler quotes with approval Sir William Jenner's manner of applying a turpentine stupe, which was as follows: A flannel roller was placed beneath the patient, and then a double layer of thin flannel, wrung out of very hot water, with a drachm of turpentine mixed with the water, was applied to the abdomen and covered with the ends of the roller. When turpentine is given by the mouth ♏ vi.–x. every three or four hours is a suitable dose, and ℨ i.–ii. twice a day when given by enema. Asafœtida may be added with advantage to the enema, or given in pill or emulsion by the mouth. The excessive meteorism is often the result of fermentative

processes in the bowel. In such cases intestinal antiseptics, such as beta-naphthol, salol, or charcoal, should be given. The abdominal pain caused by the distended bowel may require the use of an opiate. The gas is mainly confined to the large intestine, and much relief is often gained by passing the rectal tube high up into the colon. This procedure may be repeated once or twice a day and large quantities of gas drawn off. If this measure fails it may be necessary to resort to puncture of the colon. This operation is, of course, attended with considerable danger to the patient and by some authorities is not believed to be justifiable. Dalgliesh, however, has recently reported a case in which a fatal issue was averted by puncture of the transverse colon. The patient was in a condition of collapse, the abdominal tympanites being extreme. The transverse colon was distinctly delineated running across the abdomen. The introduction of a long tube through the rectum led to copious evacuation of typical pea-soupy fluid, which was horribly offensive. Its removal, however, afforded no relief, so that a trocar and a cannula were pushed into the dilated colon. On removing the trocar much gas escaped with a loud, hissing noise, continuing for two minutes. There was immediate relief to the distention, and the general condition improved remarkably. The tympanites later recurred to some extent. The patient had one rather profuse intestinal hemorrhage and a series of chills, which responded to quinine. Recovery was eventually complete. When the tympanites is due to debility and to a paretic distention of the bowel it is to be met by free stimulation with whiskey and by the use of strychnine in full doses.

Diarrhœa is usually controlled with little difficulty. A moderate diarrhœa—two to four stools in the twenty-four hours—is beneficial to the patient and should be encouraged, in my opinion, rather than checked. The older writers looked upon diarrhœa as a formidable symptom, and the influence of their teachings is still shown in the practice of many physicians at the present day. The view is, however, slowly gaining ground that diarrhœa should properly be regarded as an effort of nature to get rid of the poisonous products of the disease, and that in itself it is not to be feared. As I have already stated, diarrhœa artificially produced by the use of laxatives from the beginning of the disease does no harm to the patient. If the movements exceed four a day, bismuth may be given in rather large doses. Opium in small doses (gr. $\frac{1}{6}$–$\frac{1}{4}$) may be added to the bismuth, but care should be taken not to produce constipation. Sometimes excessive diarrhœa is caused or aggravated by improper food. If an inspection of the stools shows the presence of curds the diet should be changed or restricted.

Constipation, in my experience, requires attention more frequently than diarrhœa. If a patient is brought under treatment early in the course of the disease, and is placed upon a carefully regulated diet, days may pass without an evacuation of the bowels, unless laxatives or enemata are given.

Intestinal hemorrhage should be treated by absolute rest, cold to the abdomen, and full doses of acetate of lead and opium. Rest is the most essential part of the treatment. If the hemorrhage is profuse, it may be well to dispense with the bed-pan and allow the patient to pass the motions into the draw sheet or a folded cloth. Cold may be applied to the abdomen by the Leiter coil or by means of light ice-bags. The diet should be temporarily restricted and all food and drink given cold. Cracked ice may be given freely. Hare recommends the use of Monsel's salt (ferri subsulphas) as follows: Three grains made into a pill should be given every half-hour or oftener, the pill being made hard enough to reach the intestine without being dissolved and its contents decomposed in the stomach. Ergot is advocated by many writers but is of doubtful value except perhaps in the lighter hemorrhages early in the disease. If the bleeding is from an eroded artery it may even be increased by the constricting action of the ergot upon the arterioles beyond the bleeding point. Osler thinks that the patient may be spared the usual styptic mixtures with which he is so often drenched. I have never felt the need of using anything but the acetate of lead and opium already mentioned. If there is a tendency to collapse stimulants should be given freely. Stewart advises the hypodermic use of nitroglycerin (gr. $\frac{1}{50}$) in a syringeful of ether. Strychnine should be given in the same manner. If the loss of blood has been great, the foot of the bed should be raised and normal salt solution given by hypodermoclysis or by rectal injection.

Peritonitis, whether due to perforation of the intestine or to other causes, is to be met by the free use of opium. Absolute rest must be maintained and the amount of food and drink reduced to a minimum. Cold should be applied to the abdomen, especially to the right iliac region. Should the symptoms point to perforation a surgeon should be associated in the case and the advisability of laparotomy considered. Peritonitis in the large majority of cases is caused by perforation of the intestine or of the gall-bladder, and in either event surgical interference offers the most hope for the patient. Keen, in his study of the subject, collected 83 cases of laparotomy after typhoid perforation of the intestine. In the 83 cases there were 16 recoveries and 67 deaths, or a mortality of 80.64 per cent. as compared with 90 to 95 per cent. of deaths after perforation without operation. J. E.

Platt has recently collected 20 cases in addition to those reported by Keen, making 103 in all, with 21 recoveries and 82 deaths, thus reducing the death rate to 79.62 per cent. Platt believes that if operation were undertaken within twenty-four hours of the time of perforation recovery would follow in from twenty-five to thirty per cent. of the cases in which without operation a fatal result would inevitably occur. When perforation of the gall-bladder takes place laparotomy is even more strongly indicated. There are 30 recorded cases of this accident, 4 of which were operated upon. Three of the 4 patients recovered, whereas the remaining 26 all died.

The time of operation after perforation of the intestine must be wisely chosen. According to Keen, the best time is not during the immediate primary shock which lasts during the first few hours. An analysis of the cases shows that the second twelve hours after perforation is the most favorable period. There should then be no further delay. "The earliest moment at which the operation can be done after the immediate shock of the perforation, provided, of course, there has been any shock, as is sometimes not the case, the better it will be for the patient. Every hour then counts, since the infection of the peritoneum becomes more diffuse and more intense" (Keen). In the cases operated upon within twelve hours, the percentage of recoveries was 26.7 per cent.; between twelve and twenty-four hours, 30 per cent. After twenty-four hours the mortality was almost total. Keen therefore lays down the rule that *if the operation is not done within about twenty-four hours after the perforation there is practically no hope of a recovery.*

Cardiac weakness is to be met by the free use of alcohol and strychnine. If the case is urgent, strychnine should be given hypodermically in doses of gr. $\frac{1}{30}$ – $\frac{1}{20}$ every four hours. Caffeine is also a valuable remedy, and may be given in addition to the strychnine. Digitalis is advised by many writers, but should be employed with great caution, if at all, as it is a dangerous stimulant to the heart when degeneration of the myocardium exists. In sudden cardiac failure nitroglycerin is of great service, and may be given hypodermically in doses of gr. $\frac{1}{50}$ in alcohol or ether. If the weakness of the circulation is extreme, the patient should be kept in the recumbent position with the foot of the bed raised and the pillows removed. J. C. Wilson also recommends the application of sinapisms or turpentine stupes to the præcordia and epigastrium.

Typhoid affections of the bones require prompt and thorough surgical treatment. As has already been stated, necrosis and periostitis are the most frequent forms of bone disease. "When fluctuation can be perceived, unquestionably immediate operation should be done.

It is better, however, to operate even before fluctuation arises unless spontaneous resolution is fairly certain to follow. By such early interference suppuration may be avoided and the case cut short" (Keen).

Fortunately, surgical treatment in most cases is needed, not during the typhoid attack, but after return to health.

Management of Convalescence.

The management of the diet is our chief concern during convalescence. The change from fluid to solid food should be made very gradually. In my opinion solid food—meaning thereby meat—should not be permitted until the evening temperature has been normal for at least a week. Some practitioners allow it on the disappearance of the fever, others as soon as the patient becomes hungry, provided the temperature is within fairly normal limits and the other symptoms are favorable. But little good is accomplished by such early indulgence of the appetite of the patient, and irreparable harm may be done. Semisolid food, however, such as soft-boiled eggs, milk toast, and baked custards, may be allowed within two or three days after the fever subsides. One egg may be given on the first day, then if no harm results, two eggs on the second day, always allowing a sufficient interval of time to elapse to note any rise of temperature or other unfavorable symptoms. Farinaceous foods—rice, tapioca, farina, wheatena, etc.—may next be added to the diet. At the end of a week or ten days a little meat may be allowed. Scraped beef made into a sandwich with bread is much used in the New York hospitals as an introduction to solid food. The following diet table is given by Gilman Thompson as suitable for the convalescence of typhoid fever, beginning two or three days after disappearance of all fever:

First Day.—Chicken broth thickened with thoroughly boiled rice; milk toast or cream toast. Once only during the day.

Second Day.—Junket, mutton broth, and bread crumbs; milk toast. A piece of tender steak may be chewed, but not swallowed.

Third Day.—A small scraped-beef sandwich at noon. A soft-cooked egg or baked custard for supper.

Fourth Day.—The soft part of three or four oysters. Meat broth thickened with a beaten egg; cream toast; rice pudding or blancmange and whipped cream, or Bavarian cream.

Fifth Day.—Scraped-beef sandwich; a tender sweetbread. Bread and milk. A poached egg. Calf's-foot jelly.

Sixth Day.—Mush and milk, scrambled eggs, chicken jelly. Bread and butter.

Seventh Day.—A small piece of tenderloin steak, or a little breast of broiled chicken. Bread and butter. Boiled rice. Wine jelly. Sponge cake and whipped cream.

Eighth Day.—A slice of tender, rare toast beef, a thoroughly baked mealy potato served with butter or mashed with cream. Other foods as before.

Ninth Day.—A little broiled fresh fish for breakfast. Beefsteak at dinner. Rice, macaroni, eggs. Sago, rice, or milk pudding; a baked apple.

Tenth Day.—Mush and milk; a squab or breast of partridge or roast chicken. Other foods as before.

In severe cases, in which much alcohol has been used, it is usually necessary to continue stimulation for some time after subsidence of the fever. Wine or beer or whiskey may be used, taken preferably with the meals. Thompson thinks it well to give a little alcoholic stimulant if there is much difference in the frequency of the pulse between lying down and sitting or standing, or if the pulse is very slow. Bradycardia is very common in convalescence from typhoid fever. Osler has counted the pulse as low as 30, and states that instances are on record of still fewer beats to the minute.

Towards the end of the first week of normal temperature the patient may be allowed to sit up in bed for a half-hour or an hour each day. During the course of the second week he can usually sit in a chair or lie on a sofa for a part of each day without ill effect. Indeed, getting the patient out of bed often has a beneficial effect upon his digestion and causes him to sleep more soundly. Sometimes, especially when the attack has been protracted and severe, the temperature keeps up long after the morbid process has terminated. Da Costa and Musser have called particular attention to this class of cases, terming them cases of "bed-fever." In these cases the fever is due to exhaustion, lack of food, and long continuance in bed. The use of stimulants, solid food, and getting the patient out of bed bring the temperature to normal.

The patient should be carefully guarded against all unnecessary excitement or emotional disturbance. A recrudescence of the fever often follows upon the first visit of sympathetic friends or relatives. Murchison reminds us that the liability to perforation, hemorrhage, or a relapse, when convalescence appears to be progressing favorably, must always be kept in view, and in every case it is important to continue taking the temperature once every evening for at least two weeks after the commencement of convalescence. When convalescence is slow, a change of air and scene is indicated.

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